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THE AMERICAN
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VOL. 105 JULY, 1933 No. 7

# EDITORIAL

## APPLE LAUNDERING

THE ancient adage

*"An apple a day, keeps the doctor away"*

antedated both the vegetarian vows of Fletcher and the drugless dogmas of the Eddyists. Nor is it a slogan styled by an association of enterprising fruit growers bent on making the world apple conscious. Rather it is the rhyming reaction of someone who long ago crystallized in words the fundamental findings of an instinct-guided countryside.

And proverbs of this wise are mostly dependable and true, although they may not be nearly as euphonious or clever as are the trade slogans of today, tempered to some special purpose.

Ever since Eve made the apple of Eden a symbol of lasting employment—and so slandered its services—the apple, in spite of such handicap, is everywhere held in esteem.

It has furnished the healthy, healthful food and drink of countless generations. Young and old relish it and recognize its value—and in its diversified kinds, from the sour crab to the succulent winesap, democracy favors its flavor and finds it a form of insurance.

Yet the apple has recently come upon harrowing times. For man is not the only creature with an apple appetite. Other insects have learned to love it and the tree that gave it birth. No fruit tree today is subject to such a variety of insect menaces as is the old apple tree.

No tree has been more inbred and altered, with a consequent lack of resistance. Since the primitive Johnny Appleseed spread his practical gospel over Ohio way—much change has come to the apple—much improvement in flavor and texture, but a greatly lessened resistance. And to save his beloved fruit from insect extinction, man has had to resort to all manner of preventive sprays and dusts and poisons.

Today it looks as if he has won a partial victory, even though he continues to wage a tedious, torrid battle.

Arsenic, the far-famed poison of history, once the toxic tool of courts and embassies, latterly gutterized to poison rats—has become the successful weapon of defense in man's fight for his precious apple.

And it is this wide use of arsenic in apple tree sprays that brings our ancient adage back into the picture again—though with variation,

*"An apple a day, may bring the doctor your way"*

—except that fortunately, as usual, the lynx-eyed chemists of the Federal force were quick to sense the danger and as quick to circumvent it. For of the arsenic used to kill the bugs much remained on the skin of the apple—and was a potential danger to every consumer.

As high as a grain (a fatal dose) of arsenic has been reported on a single apple, and one can only guess as to what damage was done before the government insisted upon the thorough removal of poison residues. This removal of arsenical residues is not a perfunctory, haphazard job. It must be thorough.

Today apples are forbidden in interstate sale if they contain more than 1/100th of a grain of arsenic to the pound, a quantity obviously harmless. But how to dispose of these residues was the problem. And here is how the fruit of democracy is today made safe for little Johnny; not particularly appetizing to read about, but at least satisfying from a safety-first standpoint.

One method of washing involves the use of muriatic acid (1 per cent. at 120 degrees F.), and another uses a silicate of soda at about the same temperature, frothing of the bath being prevented through the addition of kerosene. And this detergency must be complete, for the oil sprays and the apple wax bind the arsenic quite firmly to the skin.

Of course one finds it difficult to associate muriatic acid and silicate of soda and kerosene with the time honored orchard comestible —but better a laundered apple than an arsenic tainted fruit.

All of which suggests that the so-called forward march of our civilization is often more of a retreat than a march, and always in the face of tremendous odds.

We pollute our rivers with all manner of filthy sludge and sewage—and then proceed to remove the contaminants so as to secure for our city-packed people, a drinkable Adam's ale—well chemicalized in the bargain.

We grow a bumper crop of wheat full of things-of-the-sun—we grind it and mill it and bleach it, and send most of its sunshine away—just for the sake of elegance—a silly insistence on white—while the less white whole wheat is far healthier.

Yet neither the pollution of our waters nor the bleaching of our wheat is necessary.

Both are ridiculous!

But the apple laundering is another story. To make that friendly fruit safe for democracy we must first foil the pests—even with as dangerous a material as arsenic—and then find our safety in scrubbing—and scrubbing well.

But withal, we cannot refrain from suggesting that Galileo was subtle when he murmured at his famous or infamous trial *"E pur si muove"* (the world does move).

HE DID NOT SAY IN WHAT DIRECTION!!

IVOR GRIFFITH.

---

DISTILLATION SEPARATES LIGHT FROM HEAVY WATER.—Distillation and adsorption can now be used to concentrate heavy weight water out of ordinary water, Drs. Edward W. Washburn and Edgar R. Smith, of the United States Bureau of Standards, have determined.

Electrolysis was the earlier method used by Dr. Washburn and his associates to manufacture water heavier than normal. The common sorts of hydrogen and oxygen, masses 1 and 16, are given off first as gases in electrolysis, leaving the remaining water rich in the double weight hydrogen and the heavier oxygen isotopes 17 and 18.

Because the heavy water so made was found to have a higher boiling point, Dr. Washburn realized that it should be possible to fractionate water by distillation. He distilled ten quarts and the two portions were found to differ in density by sixty-five parts per million.

Water was also fractionated by allowing a mass of activated charcoal to stand for three weeks in water. The adsorbed water was denser than that unadsorbed.—*Science News.*

## WANTED—A LEADER

"LIKE a ship with an empty pilot house floundering in a fog" has been tersely stated to be the condition of present-day pharmacy. It is probably a fairly true statement; there is no one actually steering the ship.

Someone has said that we have "fallen apart into groups, classes, blocks, sects and insects." Manufacturers come together divided into groups. Makers of chemicals, pharmaceuticals, proprietary and semi-proprietary preparations, manufacturers of cosmetics and disinfectants, makers of all sorts of compounds, wholesalers, chain stores, syndicate stores, and dealers of many sorts form other classes and groups; always one group separated from the others—sometimes divided amongst themselves. We have in our calling no leaders, no united front. In convention assembled we listen to spell-binding oratory, pass resolutions, endorse legislations, and go home again. Out of it there arise no leaders who lead. Even our splendid journals are not leaders. Among them are excellent specimens of modern journalism and fine examples of the printer's art, but they are so numerous and so voluminous that we may fear that few "read, mark and inwardly digest," and that fewer still follow their teachings. We have many, perhaps too many, writers—able, sincere, earnest gospellers and preachers—but for the most part they are without followers.

Perhaps we write too much, print too much, read too much and do too little. Scholarship we have, and in truth we are making scientific progress. Pharmaceutical education is advancing. But our scholars, our professors, our men of high attainments are not born to be leaders and they do not lead. Perhaps we have too many pharmaceutical politicians, but are lacking in pharmaceutical statesmen. A politician is defined as a man who puts his ear to the ground and finds out what his constituents want and helps them to get it. On the other hand, the statesman finds out what people really need and helps them attain that need. We need leaders who are real leaders, who do their own thinking and who can think in terms of the whole realm of pharmacy. We need authority based on granite sound convictions, not on opinions or feelings.

"Pharmacy first" is a slogan that needs to be made the foundation of every association, group or organization. It should be

written on the walls of every college, school and store and in the hearts of every man who follows the calling. In our tragic and bewildering situation we need the authority of vision, knowledge, conviction and faith. We need men who not only see problems, but see through problems; men who have not only sight, but insight; men with open eyes and open hearts who see enough and are good enough to be real leaders.

When a real leader is found he must have followers. Authority must be recognized and obeyed. Localized group and self-interest must be sacrificed for the good of the whole; else, progress will cease and success will be impossible.

With courage, faith and hope we can emerge from the turmoil and complexities which now encompass our calling. We may not need a dictator, a Mussolini, a Hitler, or even a Roosevelt, but we do need a leader who will lead.

FRED B. KILMER.

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TREATMENT OF VINCENT'S ANGINA—H. Downer in the course of a paper on Vincent's angina, states that the treatment of an attack is the exhibition of arsenic combined with rest in bed. All forms of arsenical preparations can be used, but the most convenient and efficient is sodium cacodylate given hypodermically, at twenty-four hour intervals, for a week or ten days. Local applications of arsenic are invaluable, preceded by thorough cleansing with peroxide. The form of arsenic again is of little importance, and liquor arsenicalis, B. P., painted on the infected areas is efficient and satisfactory. Sodium perborate can take the place of peroxide of hydrogen, and a mouth-wash of equal parts of liquor arsenicalis and ipecacuanha wine is of value but will not reach ulcers on the tonsils or pharyngeal wall. Treatment must be carried out at least after every meal and last thing at night. If the cervical glands are enlarged and tender, antiphlogistine compresses are invaluable. The pain in swallowing can be relieved by aspirin or by a spray containing antipyrine and salicylic acid.—"British Dental Journal," 53, 9, 407, through *Chemist and Druggist*.

# ORIGINAL ARTICLES

## A SIMPLIFIED AND MORE EFFICIENT METHOD FOR THE EXTRACTION OF CAPSAICIN TOGETHER WITH THE COLORIMETRIC METHOD FOR ITS QUANTITATIVE DETERMINATION IN CAPSICUM FRUIT AND OLEORESIN

**A THESIS**

**Presented to the Faculty of the Philadelphia College of Pharmacy and Science**

**By Linwood F. Tice**
**Candidate for the Degree of B. Sc. (Pharmacy)**

### Isolation of Capsaicin

VARIOUS methods for the extraction of capsaicin, the active constituent of capsicum, have been reported.[1] All of these methods were found to be exceedingly tedious and time consuming or they yielded a product which was highly colored and more or less impure.

A new method was devised which embodies certain steps in the older methods but which is by far to be preferred, inasmuch as it yields a snow-white crystalline product and the procedure is considerably shortened.

The method of extraction is as follows:

I. Take approximately 100 gm. of oleoresin of capsicum (Mombassa), place in a large separatory funnel and add 2 x its volume of heavy liquid petrolatum. Shake well until thoroughly mixed.

II. Extract with three 200 cc. portions of 57 per cent. alcohol and mix these extractions.

III. Add to this alcoholic extract 100 cc. of heavy liquid petrolatum, shake well in a separatory funnel, allow to separate, and draw off alcoholic layer.

IV. Distill off alcohol, cool and extract the aqueous liquid with ether avoiding any loss of oily residue left in the flask which is ether soluble. (Sodium chloride added to the aqueous portion will prevent any troublesome emulsification encountered during this step.)

V. Evaporate the ether leaving an oily residue; add 4 gm. Li $(OH)_2$ (carbonate free), 200 cc. water and boil for 10 minutes with occasional stirring.

VI. Allow to stand over night, then pass in $CO_2$ intermittently for two hours, adding water if the liquid becomes too thick, and let stand over night.

VII. Filter through a Buchner filter, wash precipitate with water and dry at a low temperature.

VIII. Place precipitate on filter into a large flask and boil with 500 cc. of petroleum ether for 15-20 minutes using a reflux condenser and occasionally agitating the material by rotating the flask.

IX. Pour the petroleum ether while hot through a filter paper and set the clear filtrate in a sub-zero refrigerator over night to effect crystallization. Reserve all undissolved material on filter for subsequent petroleum ether extraction.

X. Filter chilled petroleum ether quickly through a small plain filter or a Buchner, collect crystals, dry, transfer to vial and tightly stopper.

The precipitate (VIII) can be repeatedly extracted with the same petroleum ether and the capsaicin subsequently crystallized out by chilling. However, if the petroleum ether after repeated use becomes markedly yellow, it should be discarded and a fresh lot substituted; otherwise, the crystals yielded will be faintly colored.

The filter paper and funnel used in IX should be saved, covered with a glass plate, and used to filter successive hot petroleum ether extractions.

Employing the above method and starting with 100 gms. of Mombassa oleoresin at least 5 gm. of capsaicin should be obtained, providing several extractions of the precipitate (VIII) are made.

A brief explanation of the steps is as follows: The heavy liquid petrolatum serves to withhold much fixed oil and coloring matter, then by distilling off the alcohol and extracting with ether any water soluble materials are eliminated. The "oily" liquid left after the ether evaporation is impure capsaicin which when boiled with Li $(OH)_2$ solution forms a water soluble lithium capsaicin. This is decomposed and capsaicin is precipitated in crystals by the action of $CO_2$. Then the dried precipitate is extracted with hot petroleum ether in which it is somewhat soluble, and upon chilling the petroleum ether, its solvent power decreases; thus capsaicin crystallizes out.

The capsaicin obtained by this process gave all the identity tests reported and was found to possess a sharp melting point of 64 degrees C.

Attention is called to the extreme pungency of capsaicin (1-10,000,000 detectable in throat) and although it is not volatile the small crystals are so fluffy that they are carried mechanically into the air upon the slightest disturbance. Therefore, capsaicin in crystalline form should be transferred from one container to another under a hood or violent sneezing and coughing will result.

### The Colorimetric Assay

The reaction of capsaicin with vanadium oxytrichloride was reported by Fodor [2] who outlined a brief method for the assay of the capsaicin content of capsicum based on this reaction. A study of his method was made for the purpose of adapting it for use on capsicums many times more pungent than those used in his experiments. Certain changes and refinements have been made which enable one to satisfactorily employ this method to supplant the unscientific organoleptic tests which are quite inaccurate, realizing the inconsistency of taste in a quantitative determination.

The assay is of a colorimetric nature depending upon the reaction of vanadium oxytrichloride ($VOCl_3$) with capsaicin producing an intensely blue compound vanadyl capsaicin, $C_{18}H_{26}NO_3$—$VOCl_2$ (Fodor). The absence of water must be maintained throughout, using dry chemicals and apparatus, as water destroys the vanadium salt and densitizes the color reaction.

The following substances should be available:

1. Vanadium oxytrichloride C. P.—This should be kept in small bottles with greased glass stoppers in a desiccator.
2. Carbon tetrachloride C. P.
3. Dried Acetone—Dried over $CaCl_2$ and distilled.
4. Paprika—Free of pungency.
5. Capsaicin—This can be readily obtained by the process given. It should be a white crystalline solid with a sharp melting point of 64 degrees C.

The drug is assayed by first obtaining a representative sample. If the drug be whole, this is not difficult; if it be ground care should be taken in sampling not to collect either all fine portions, which consist largely of placentae and contain most of the activity, or all coarse particles, which consist of seeds and pericarp, and contain but little.

The sample is preferably dried over night in a desiccator. A 2 per cent. w/v extraction of the drug is made by macerating the drug from 30 to 60 minutes with dry acetone in a stoppered flask with occasional agitation. If the oleoresin is to be assayed a 0.2 per cent. solution of the oleoresin is made in dry acetone.

A solution of the active principle is now prepared 0.02 per cent. in dry acetone, colored by extracting sufficient capsaicin-free paprika to produce a color depth approximating that of the 2 per cent. extract of the drug to be assayed. The use of a dried acetone w/v extract of paprika as the solvent in preparing this standard was found to result in a closer matching of the unknowns with the standards, the reason being that the $VOCl_3$ reacts with the coloring principles of both capsicum and paprika similarly. The amount of paprika needed will vary between 0.1 per cent. and 0.2 per cent. depending upon the amount of color in the capsicum to be assayed.

A series of standard tubes are prepared by measuring from a burette the correct quantity of the 0.02 per cent. solution of capsaicin in colored acetone and diluting to 5 cc. with colored acetone.

The standard tubes are prepared by the following chart:

| *0.02% capsaicin in colored acetone* | *Colored acetone* | *Capsaicin content of standard tube* |
|---|---|---|
| 1.5 cc. | 3.5 cc. | 0.006% |
| 2.0 cc. | 3.0 cc. | 0.008% |
| 2.5 cc. | 2.5 cc. | 0.010% |
| 3.0 cc. | 2.0 cc. | 0.012% |
| 3.5 cc. | 1.5 cc. | 0.014% |
| 4.0 cc. | 1.0 cc. | 0.016% |
| 4.5 cc. | 0.5 cc. | 0.018% |
| 5.0 cc. | 0 cc. | 0.020% |

The standards are put in a rack in sequence and are immediately followed by the tubes containing the unknowns. Beginning with the first of the standards one drop of a 1 per cent. solution by volume of $VOCl_3$ in $CCl_4$ is added to each tube for each thousandth of a per cent. of capsaicin known to be present using an ordinary medicine dropper to add the reagent. The reagent is then added to the unknowns, carefully, drop by drop, until no deepening in blue color is noticed. If an excess of reagent is added the liquid turns green and cannot be matched with the standards as the color is not of the same

quality. Consequently, it is advisable to take several tubes of the same unknown and add a different number of drops in each and then select for matching the tube having the greatest depth of blue but no suggestion of green. When experience is obtained this procedure will not be necessary as the worker soon learns when a sufficient amount of reagent has been added to the unknowns. The reagent must be added to all tubes both standards and unknowns without appreciable time elapsing between the additions as the color slowly fades after its production. To add the reagent to the standards and then in 15-20 minutes to the unknowns would invalidate the analysis.

The unknown tube having the greatest depth of blue is now matched with the standards and that standard found which has the nearest color depth to it. In cases where the unknown tube lies between two standards it is assigned a value correspondingly—e. g., an unknown tube darker than 0.010 per cent. and lighter than 0.012 per cent. would be given a value of 0.011 per cent. This increases the accuracy of the determination.

The matching is best accomplished by looking down through the tubes at a source of diffused illumination such as a frosted incandescent bulb.

A flat bottom 10 cc. glass tube with an internal diameter of about 11 mm. provides the best tube to be used for the work. A matched set for height of 5 cc. was obtained and used in this study.

After estimating the per cent. capsaicin in the unknown tube, this figure is multiplied by the dilution factor 50 in case of the drug, and 500 in case of oleoresin. This results in the per cent. capsaicin present in the sample.

If the sample produces an unknown tube falling either below or above the standards in intensity of color, repeat the assay using a higher or lower concentration of the sample in acetone, instead of preparing lower or higher standards, as it is difficult to compare color depths lower or higher than those of the standards given.

Several varieties of capsicum were assayed and the capsaicin content found to vary over wide limits from less than 0.1 per cent. to as much as 1.0 per cent. It was also found that within a single variety there is considerable fluctuation. Mombassa capsicum was found to be unquestionably superior to all others in capsaicin content both in the drug itself and the oleoresin prepared from it.

It was definitely verified by the colorimetric examination of capsicum that the placenta contains the preponderance of the active prin-

ciple, as has been previously reported. The cortex contains only a small amount and the seeds practically none.

Oleoresins made by extraction of capsicum with carbon tetrachloride were shown to be decidedly inferior to those made by the use of acetone or ether. Such oleoresins not only were subject to rapid color deterioration but they also were deficient in capsaicin content. The use of metallic apparatus in conjunction with carbon tetrachloride is particularly deleterious to capsaicin, and copper seems to be the worst offender in this respect.

It was observed that vanadium oxytrichloride reacts with various other phenols. It is suggested that some interesting experiments could be conducted to attempt the utilization of the vanadium method in the assay of phenols other than capsaicin.

## Summary

1. A more satisfactory technique for the isolation of capsaicin is presented,

2. The details of the vanadium colorimetric assay method for the capsaicin content of capsicum are outlined, and

3. Some observations made during this study of general interest concerning capsicum are included.

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(2) *Zeits. f. Unters. d. Lebensm.*, Sept. 26, 1930.

# THE IDENTIFICATION OF COCAINE AND NOVOCAINE

*(To be continued.)*

**By Charles C. Fulton**

**Associate Chemist, United States Industrial Alcohol Laboratory, Minneapolis, Minn.**

THE laboratories of the U. S. Industrial Alcohol Bureau examine samples of illegal cocaine seized by the Narcotics Bureau. During the last two years or so a large part, perhaps most, of this cocaine has been adulterated with novocaine. There have also been cases of complete substitution of novocaine for cocaine. Novocaine is not subject to the Federal law which regulates the sale and possession of the alkaloids of opium and coca leaves. It is therefore necessary that the government chemists be able to identify both cocaine and novocaine separately and also be able to prove beyond question the presence of cocaine in mixtures of the two. Others may be interested in the tests for these alkaloids, and in the discussion of general precipitation methods which are applicable to all amines.

## Tables of Precipitation

The two following tables give pictures of the relation of cocaine and of novocaine to the alkaloidal precipitating agents. The sensitivities are stated and the reagents giving crystals are underlined.

General information about the reagents, and the exact formulas for most of those used in this study, will be found in my article "The Precipitating Agents for Alkaloids." [1]

## Explanations of Tables

The reagents giving crystals are underlined. Only amorphous precipitates have been observed with the others, but it is probable that crystals can be obtained in a few other cases by special treatment, such as warming.

The arrangement of the reagents in columns, and the numbers attached to each, pertain to the sensitivity as compared with that of phosphomolybdic acid. Starting with the strongest solution of the alkaloid a series of solutions was prepared by repeatedly doubling the volume of a part of the solution. The last solution of this series to

(1) *American Journal of Pharmacy*, April, 1932.

## COCAINE

(Alkaloid Dissolved in Dilute Acetic Acid)
(Or Hydrochloride in Neutral Water)

solution 1, about 1:2500

Phosphomolybdic acid—1
Phosphotungstic acid—1
Silicotungstic acid—1
Bromine in NaBr—¼
Bromine in HBr—¼
Bromine water—¼
Wagner's No. 1—1/16
Wagner's No. 4—1/16
Wagner's No. 6—⅛
Wagner's No. 8—¼
Iodine—NaBr—⅛
Iodine in excess NaBr—½
Dragendorff's—⅛
Dragendorff & KI—⅛
Mayer's—⅛
Concd. Mayer's—⅛
Mayer's & KI—½
Marme's—1 to ½
Cadmium iodide—1
Stannous Na Iodide, acid—¼
Lead Na Iodide—½
Antimony K Iodide, acid—¼
Platinum iodide in excess NaI—1
Platinum Na Thiocyan.—½
Mercuric K Thyocyan.—1
Zinc Na Thiocyanate—1
Stannous Na Thiocyanate acid—¼
Gold Bromide—½
Gold bromide & HCl—½
Bismuth bromide in HBr—½
Mercuric Na Bromide—½
Bromomercuric acid—½
Gold Chloride—½
Gold Chloride & HCl—1 to ½
Tannic acid & NaAc—1

Nessler's—2
Silver Na Iodide—2
Zinc K Iodide—16
Reinecke's Salt—2
Cobalt Na Thiocyan.—4
Cadmium Na Thiocyan.—8
Ferric Na Thiocyan.—2
Manganous Na Thiocyan.—4 to 8
Stannous Na Bromide, acid—2
Mercuric bromide—16, 8
$HgBr_2$ in HCl—4
$HgBr_2$ in NaBr soln.—4
Cadmium Na Bromide—8
Platinum Bromide—4
Platinum bromide & HCl—8
Mercuric Na Chloride—4
Chloromercuric acid—4
Mercuric chloride—16
$HgCl_2$ in HCl—16
$HgCl_2$ in NaCl soln.—16
Platinum chloride—16
Platinum chloride & HCl—16
Palladium chloride—16
Stannic chloride in HCl—16
$SnCl_2$ in HCl—16
$FeCl_3$ in HCl—8
Picric acid—2
Na Picrate—4
Tannic acid—8
Alizarin Na Sulfonate—16
Trinitroresorcin—4
$NH_4$ Molybdate—4
Na Phosphomolybdate—8
Chromic anhydride—16
Concd. $CrO_3$—8
$CrO_3$ & HCl—4
$CrO_3$ in NaCl soln.—4
$KMnO_4$—about 8 to 16
Sodium carbonate—4
Sodium hydroxide—8
Ammonia—8
Potassium cyanide—8
Gold Cyanide—8
Platinum Cyanide—4
Mercuric Na Chloro Nitrite—8

strongest solution about 5%, soln. 128

Concd. KI—128
5% KI—no ppt.
Nickel Na Thiocyan.—32
$NH_4SCN$—128
Concd. $FeCl_3$—128
$BiCl_3$ in HCl—32
$SbCl_3$ in HCl—32
$ZnCl_2$ & HCl—128
$CdCl_2$ & HCl—no ppt.
Zinc chloride—no ppt.
Cadmium chloride—no ppt.
Saccharin—no ppt.
p-Nitrophenol—32
Picrolonic acid—no ppt.
$K_2Cr_2O_7$—64
Perchloric acid—16 to 32
Na Perchlorate—32 to 16
Potassium chromate—128
Concd. K Acetate—no ppt.
$Na_2HPO_4$—no ppt.
Na Nitroprusside—64
K Ferricyanide—128
K Ferrocyanide—no ppt.
Mercuric Na Nitrite—128
Na Cobalti-Nitrite—32
Lead Copper Sodium Nitrite—no ppt.
Lead Na Nitrite—no ppt.

## NOVOCAINE (Hydrochloride in Water)

solution 1, about 1:8000

Phosphomolybdic acid—1
Phosphotungstic acid—1
Silicotungstic acid—1
Bromine in NaBr—¼
Bromine in HBr—¼
Bromine water—½
Wagner's No. 1—¼
Wagner's No. 3—½
Wagner's No.4—1 to ½
Wagner's No. 5—1 to 2
Acid Wagner's No. 1—¼
Dragendorff's—½ to 1
Dragendorff's & KI—1 to 2
Mayer's—1 to ½
Concd. Mayer's—½
Gold Bromide—1
Bismuth Bromide in HBr—1
Gold Chloride—1
(with short standing; 4 immediately, 2 quickly)

Wagner's No. 6—2
Wagner's No. 7—4
Wagner's No. 8—8
Acid Wagner's No. 3—2
Acid Wagner's No. 5—16
Iodine-NaBr—4
Iodine in Excess NaBr—16

Acid Mayer's—4
Mayer's & KI—8
Marme's—8
Cadmium Iodide—16
Lead Na Iodide—4
Silver Na Iodide—16
Antimony K Iodide, acid—8
Platinum Iodide & Excess Na I—4 to 8
Platinum Na Thiocyanate—2
Acid Platinum Na Thiocyanate—4
Reinecke's Salt—16
Mercuric K Thiocyan.—8
Acid Mercuric K Thiocyanate—16
Zinc Na Thiocyanate—8
Gold Bromide & HCl—16 immediately, 2 gradually
Mercuric Na Bromide—4
Bromomercuric acid—16
Mercuric Bromide—16
Gold Chloride acid with $H_2SO_4$—8 immediately, 2 gradually
Picric acid—16
Tannic acid & NaAc—8
$NH_4$ Molybdate—16
Concd. $CrO_3$—64 immediately, 16 soon, 8 gradually

strongest solution about 1:16, soln. 512

Acid Wagner's No. 8—64
Acid Mayer's & KI—256
Nessler's—32
Acid Marme's—512
Stannous Na Iodide, acid—32
Silver Na Iodide, acid—128
Zinc K Iodide—256
Concd. KI—512
5% KI—no ppt.
Acid Zinc Na Thiocyan.—64
Cobalt Na Thiocyan.—64
Cadmium Na Thiocyan.—64
Acid Cobalt Na Thiocyanate—no ppt.
Acid Cadmium Na Thiocyanate—no ppt.
Ferric Na Thiocyan.—128
Nickel Na Thiocyan.—256
Manganous Na Thiocyn.—128
Stannous Na Thiocyanate, acid—128 to 256
$NH_4SCN$—256
$HgBr_2$ & $H_2SO_4$—no ppt.
$HgBr_2$ & HCl—no ppt.
$HgBr_2$ in NaBr soln.—32 to 64
Stannous Na Bromide, acid—no ppt.
Cadmium Na Bromide—64
Platinum Bromide—128 immediately, 16 gradually
Platinum Bromide & HCl—no ppt.
Gold Chloride & HCl—512
Mercuric Na Chloride—32
Mercuric chloride—64
$HgCl_2$ in NaCl soln.—128
Chloromercuric acid—128
$HgCl_2$ in HCl—no ppt.
Platinum chloride—256 immediately, 64 gradually
Platinum Chloride & HCl—no ppt.
Palladium Chloride—32
$SnCl_4$ in HCl—no ppt.
$SnCl_2$ in HCl—no ppt.
$FeCl_3$ in HCl—no ppt.
$BiCl_3$ in HCl—no ppt.
$SbCl_3$ in HCl—no ppt.
$ZnCl_2$ in HCl—no ppt.

$CdCl_2$ in HCl—no ppt.
Zinc chloride—no ppt.
Cadmium chloride—no ppt.
Na Picrate—32
Trinitroresorcin—64
Tannic acid—no ppt.
Picrolonic acid—no ppt.
Alizarin Na Sulfonate—64 (acid, 64 also)
Na Phosphomolybdate—64
Na Molybdate—no ppt.
Chromic anhydride—512 immediately, 64 gradually
$K_2Cr_2O_7$—256
$CrO_3$ & HCl—128 soon, 64 gradually
$CrO_3$ in NaCl soln.—64 grad.
Perchloric acid—no ppt.
Na Perchlorate—256
Sodium carbonate—64
Ammonia—64
Sodium hydroxide—64
Potassium cyanide—128
Potassium chromate—no ppt.
Concd. K Acetate—no ppt.
$Na_2HPO_4$—no ppt.
Gold Cyanide—64
Platinum Cyanide—64
Na Nitroprusside—128
K ferricyanide—256
K ferrocyanide—no ppt.
Mercuric Na Chloro-Nitrite—64
Mercuric Na Nitrite—128
Lead Copper Sodium Nitrite—no ppt.
Lead Na Nitrite—no ppt.
Na Cobalti-Nitrite—no ppt.

give an unmistakable precipitate with phosphomolybdic acid is called solution 1. It contains the unit quantity of alkaloid per unit volume, using phosphomolybdic acid precipitation as a standard. The next stronger solution contains twice as great a concentration of alkaloid and is called solution 2; the next stronger after that is solution 4. Similarly the solutions of the series beyond the limit of distinct precipitation with phosphomolybdic acid are labelled ½, ¼, and so on.

The number accompanying a reagent in the table shows the last solution in which it gives a distinct precipitate. The smaller the number, therefore, the more sensitive the reagent: the number shows how many "phosphomolybdic acid units" of the particular alkaloid are required for precipitation.

In making these sensitivity tests, let fall one full drop of reagent from a 1 cc. pipet into a drop of the alkaloidal solution of equal or only slightly greater size. Usually I make three such tests on the ordinary microscope slide. The light must be such that one can see a very finely divided precipitate. The crystal tests are, in general, also made with a full drop of reagent.

When precipitation falls off quite gradually with dilution there may be some doubt as to which solution is the last one yielding a distinct and unmistakable precipitate. However this margin of doubt is never so great as to seriously diminish the value of the scheme. Classification is based primarily on a consideration of which reagents equal or exceed phosphomolybdic acid in sensitivity and which are markedly less sensitive.[2] This is easily ascertained; when necessary a direct comparison should be made on adjacent slides between the reagent in question and phosphomolybdic acid.

In the first column of each table are listed the reagents that equal or exceed phosphomolybdic acid in sensitivity toward that alkaloid; in the second column those that are less sensitive, but still precipitate with no more than 16 phosphomolybdic acid units; and in the third column the remaining reagents.

Within the columns the reagents are written in the following order (1) Complex Oxygen acids, (2) Halogen reagents, (3) Iodides, (4) Thiocyanates, (5) Bromides, (6) Chlorides, (7) Organic reagents, (8) Simple oxygen acids, and salts of oxygen acids, (9) Basic reagents, (10) Cyanides, (11) Nitrites. This corresponds roughly to the general precipitating ability and sensitivity of the principal and better-known reagents of each group.

The Cocaine table reports the precipitation of cocaine acetate, prepared by dissolving the free alkaloid in dilute acetic acid. Substantially the same values have been found when using solutions of cocaine hydrochloride in water, in tests made both by myself and by Mr. Garvey of this laboratory.

In general it is the best practice to use the acetate of the alkaloid, with a slight excess of acetic acid, for such tests. This gives more scope for the comparison of neutral and strongly acid reagents than if a strong acid such as sulfuric is used. Hydrochloric acid in excess is out of the question, as it would greatly affect the sensitivity of most of the chloride reagents and some of the others; even the

(2) Fulton: The Identification of Alkaloids by Precipitation. *Jour. A. O. A. C.*, XIII, 4, page 491 (1930).

small amount present when the hydrochloride of an alkaloid is used will sometimes noticeably affect the sensitivity and crystallization with such reagents as $HgCl_2$, $HgBr_2$, and mercuric sodium nitrite.

The Novocaine table reports the precipitation of the hydrochloride, the usual commercial salt.

Solution 1, as noted at the top of the tables, has for cocaine a concentration equivalent to about 1 gram per 2500 cc., for novocaine about 1 gram per 8000 cc. Phosphomolybdic acid and corresponding reagents are therefore more sensitive, on an absolute scale, to novocaine. This absolute scale has to be considered in determining the possibility of detecting one alkaloid in the presence of another by precipitation. In general however the relative scale is more useful.

Using the relative scale, as is done in the columns of the tables, it will readily be seen that cocaine and novocaine belong to different classes and that cocaine is much more easily precipitated, as is shown by the greater number of reagents in the first column of the cocaine table.

It will be observed that the standard Wagner's and Mayer's reagents are more sensitive than phosphomolybdic acid to both alkaloids, but that when such reagents contain a considerable excess of KI their sensitivity toward novocaine declines to solution 8 (Wagner's No. 8; Mayer's & KI), while with cocaine they remain more sensitive than phosphomoloybdic acid. This is an important point in classification: alkaloids that resemble novocaine in this respect are easily distinguished from those that resemble cocaine.

Another class-characteristic which is quite marked and important in the case of novocaine is its lack of sensitivity to strongly acid forms of numerous reagents, particularly halide reagents containing an excess of the halogen acid, as for instance Gold chloride & HCl. This is utilized in obtaining crystals for the identification of cocaine in the presence of novocaine.

Crystalline precipitates are of course examined under the microscope. Low power is usually adequate. Characteristic crystals serve for the identification of the alkaloids.

### Descriptions of Cocaine Crystals

*Stannous sodium Iodide, acid.* Rosettes of delicate branching needles. Crystals form fairly readily in concentrated solutions and down to solution ⅛ at least; sensitive to 1:20000.

*Lead sodium Iodide.* Minute crystals, little rods in thin rosettes under high power. Test has no practical value.

*Platinum Iodide in excess NaI.* Two kinds of crystals form gradually from the amorphous precipitate; small square grains or platelets in solution 8 and more dilute; rosettes of threads in more concentrated. Crystallization is incomplete and the test has little or no practical value. Compare with the following.

*Silver sodium Iodide.* Crystals of good size form gradually from the amorphous precipitate. They are of two kinds. In the more dilute solutions, or with sufficient excess of reagent, irregular long plates, thick and grain-like, but transparent and colorless or very slightly yellowish, or colorless stick-like crystals, form in thin rosettes; best in solutions 4 and 8, especially if two drops of reagent are used. In solutions more concentrated than 16 dense dark rosettes of needles or threads are formed; these crystals are a peculiar shade of brown. Test sensitive to about 1:600. An acid form of the reagent is made by adding 2 drops of diluted sulfuric acid (1+3) to 1 cc.

*Gold Bromide* (Brom-auric acid). Feathered crystals, small needles, and splinters, often in thin rosettes or branched a little. Sensitive to solution 1/16, or about 1:40,000.

*Gold Bromide & HCl.** Similar to the preceding; crystals more needle-like, less feathery. Equally sensitive.

*Stannous sodium Bromide, acid.* Usually forms rosettes of branching threads, or branching twigs. Sensitive to solution 2, or about 1:1200. (This reagent is made by adding 4.5 gm. NaBr to 10 cc. of the same Stannous chloride stock solution used for making Stannous sodium iodide, acid.) The type of crystallization is somewhat variable.

*Platinum Bromide* (Bromo-platinic acid). Feather-comb-crystals quickly form from the amorphous precipitate. They have considerable resemblance to the well-known crystals with Platinum Chloride and constitute one of the best tests for cocaine. Characteristic crystals obtained down to about 1:1000.

*Platinum Bromide & HCl.** Similar to the preceding; crystals more comb-like, less feathery. Almost equally sensitive.

*Gold Chloride* (Chlor-auric acid).[3] Crystals form gradually from the amorphous precipitate; branching needles, small feathery crystals, and some comb-like crystals. Gold Chloride & HCl is better.

*Gold Chloride & HCl.** Crystallizes readily; small needle-like branching crystals form from the amorphous precipitate and grow to fairly large thin comb-like crystals with the teeth at an angle. There may also be rosettes of needles branching across each other. Easily sensitive to solution 1/8, or 1:20,000.

*Platinum Chloride* (Chloro-platinic acid).[3] This is generally considered the principal test for cocaine. Immediate crystallization

*These reagents contain 25 per cent. by volume of concentrated HCl.

(3) The crystals with these reagents are described and pictured by Stephenson in Some Microchemical Tests for Alkaloids. (Lippincott, 1921.)

in feather crystals, growing coarser and more comb-like on standing. Characteristic crystals obtained down to about 1:500.

*Platinum Chloride & HCl.** Similar to the preceding, but the crystals are somewhat larger, thinner, and more comb-like. Sensitive to about 1:300 (solution 8).

*Palladium Chloride* (Chloro-palladous acid).[3] Crystallization is slow and rather uncertain. Dense rosettes of needles form in concentrated solution, or with stirring. Addition of a little HCl or NaCl assists crystallization while diminishing the sensitivity. Crystals then vary to salmon-colored rods, which form in concentrated solution. Stephenson's reagent may have differed a little from mine, but in any case the test has little or no practical value.

*Stannic Chloride in HCl.* Crystals form readily; fair-sized rosettes of glassy crystals and small glassy grains. This test has a practical sensitivity of about 1:200, though small crystals form gradually down to 1:600. It is a very good test for cocaine.

*Stannous Chloride & HCl.* Crystals form gradually from the amorphous precipitate; large rosettes of branching needles. The test has no great value as crystallization is slow and it is difficult to keep the reagent without having the tin go over to the stannic form.

*Ferric Chloride in HCl.* Large splinter, blade, and fern-like crystals quickly form from the amorphous precipitate in solutions 128 to 16. There may be some rosettes of needles and splinters. The precipitate has some tendency to dissolve in more dilute solutions, although crystals can be obtained in solution 4, particularly if two drops of reagent are used. The practical sensitivity is at least 1:200. An excellent test.

*Concentrated $FeCl_3$ solution (1:1).* Large splinter crystals form, solutions 128 to 32. Similar crystals described and pictured by Stephenson were obtained from concentrated solution with 5 per cent. ferric chloride.[3]

*Antimony Chloride & HCl.* Crystallization is incomplete, but in concentrated solutions, 128 and 64, some large glassy grains are formed.

*Picric acid.*[3] The amorphous precipitate crystallizes slowly in large dense rosettes of thin needles or threads.

*Sodium Picrate.* Crystals the same as with picric acid, but form more readily. They form gradually in solution 2, slowly even in Solution 1 (1:2500).

*Trinitroresorcin.* The amorphous precipitate crystallizes slowly, or with stirring, in dense rosettes of needles or threads.

*Alizarin sodium Sulfonate.* The precipitate gradually crystallizes in brown rosettes of needles, solutions 128 to 16. Sensitive to about 1:150.

*These reagents contain 25 per cent. by volume of concentrated HCl.

(3) The crystals with these reagents are described and pictured by Stephenson in Some Microchemical Tests for Alkaloids. (Lippincott, 1921.)

*Chromic anhydride.* The precipitate given by the 5 per cent. reagent usually does not crystallize, although rosettes of threads can be obtained by stirring and seeding. *Concentrated $CrO_3$ solution* usually gives large rosettes of threads, but even with it crystallization is uncertain, and crystals may fail to form even on stirring.

*$CrO_3$ & HCl.** The amorphous precipitates, particularly in the more dilute solutions, usually yield splinter crystals, and branching needles in large growths more or less circular. Crystallization is a little uncertain.

*$CrO_3$ & NaCl.* The amorphous precipitate usually yields branching needles or threads in large growths, often rosettes.

*Perchloric acid.* The amorphous precipitate crystallizes in either of two ways: either it forms dense rosettes of needles or threads; or else it forms large colorless angular plates, and branching crystals. *Sodium Perchlorate* gives practically the same results.

*Potassium Permanganate* (slightly acid).[3] Crystals are best obtained by adding just a *small* drop of the 5 per cent. reagent with a stirring rod. Solutions 128 to 4 then give crystals, mainly square-cut reddish-lavender-colored plates. Only a few alkaloids give stable crystalline permanganates; therefore the test is a good one for *pure* cocaine; sensitive to about 1:600. Oxidizable impurities generally destroy the test. If the reagent is added as a full drop of 1 per cent. $KMnO_4$ there are obtained in addition to the plates both branching crystals and small, rather dark rosettes.

*Basic Reagents. $Na_2CO_3$, KCN, $NH_4OH$,* and *NaOH* precipitate free cocaine. The precipitate is amorphous but will generally crystallize, on stirring, in rods or peculiar floating branching forms. The precipitate with NaOH redissolves in the more dilute solutions, due to hydrolysis. $Na_2CO_3$ is a little more sensitive than the others, but perhaps KCN and $NH_4OH$ give a little readier crystallization. Crystals to about 1:300. The crystals are described by Stephenson, but not pictured.

*Sodium Cobalti-Nitrite.* Yellow rods in rosettes form in the most concentrated solutions (128 and 64).

## Descriptions of Novocaine Crystals

*Bromine in HBr* is the best bromine reagent; *Bromine in NaBr* and *Bromine water* give similar crystals but not so readily. Crystallization takes place best in concentrated solution but crystals are obtained down to solution 8 (1:1000). The crystals are white and are generally rosettes of branching needles or threads. Transparent irregular flakes or plates are also formed.

*Mayer's & KI.* In concentrated solutions white opaque roundish lump crystals grow out from a center of crystallization in rosette

*These reagents contain 25 per cent. by volume of concentrated HCl.

(3) The crystals with these reagents are described and pictured by Stephenson in Some Microchemical Tests for Alkaloids. (Lippincott, 1921.)

fashion. There are also some splinter-plate crystals. Solutions 512 to 128 crystallize in a short time; on standing crystals are formed down to solution 32 (1:250).

*Lead Na Iodide* (2 drops). Good crystallization; small transparent rods, formed down to solution 2 (1:4000).

*Gold Bromide.* Amorphous precipitate, crystallizing gradually in small to minute orange-yellow plates, often in rosettes. HCl assists crystallization and makes the crystals larger. (See following.)

*Gold Bromide & HCl.** Small orange plates, scattered and in rosettes. Solutions 512 to 16 give an immediate amorphous precipitate which soon crystallizes completely. Solutions 8 to 2 do not show immediate precipitation, nevertheless an amorphous precipitate forms first and crystallizes gradually. Crystals can be obtained in solution 1 on standing (1:8000). The best crystals are obtained near the limit of immediate precipitation (about 1:500).

*Mercuric Na Bromide.* Results similar to those with Mayers & KI. Concentrated solutions (512 to 64) crystallize in opaque rosettes in which the individual crystals seem to be small grains. Splinter-like crystals may also form. Crystals will form in somewhat more dilute solutions with stirring; or on standing the precipitate may slowly yield grains.

*Mercuric Bromide.* The precipitate gradually forms grain crystals.

*Bromomercuric acid.* Long branching needles in sheaves or rosettes. Sensitive to solution 16 (about 1:600).

*$HgBr_2$ in NaBr solution.* Forms plate-rods and branching crystals. Sensitive to about 1:150.

*Cadmium Na Bromide.* Crystallizes in branching root-like and thread crystals, or in rod-plates.

*Platinum Bromide* (Bromoplatinic acid). Probably the best crystal test for Novocaine. Small dark rosettes of needles form soon. With a little standing they are readily found down to solution 4 (1:2000). If only a very small drop of reagent is used there is immediate crystallization in light colored feathered crystals (See Platinum Chloride).

*Gold Chloride acid with $H_2SO_4$.* Although gold chloride itself gives only an amorphous precipitate, when rather strongly acidified with sulfuric acid there is partial crystallization from concentrated solutions in small grain-plates in groups or rosettes. Not a practical test.

*Gold Chloride & HCl.** One of the best tests for Novocaine. Large, irregular, coarsely feathered yellow plates, very characteristic and easily recognized. With a little standing they are formed down to solution 32 (about 1:250).

*Mercuric Na Chloride.* A concentrated solution will crystallize partially, on stirring, in grains.

*These reagents contain 25 per cent. by volume of concentrated HCl.

*$HgCl_2$ in NaCl solution.* With stirring gives crystals readily; grains and long slender rods, the latter often in rosettes. Sensitive to solution 32 (about 1:250).

*Chloromercuric acid.* Crystallizes mainly as fairly large slender rods, many in rosettes and sheaves. Grains may also form.

*Platinum Chloride.* If only a very small drop of reagent is added with a stirring rod there is *immediate* crystallization in bushy feathered crystals, irregular plates, etc., the precipitate having considerable resemblance to that of cocaine. If however a full drop of reagent is added there is immediate crystallization only in concentrated solution. Solutions 512 to 256 give coarsely feathered plates somewhat yellow in color, and other feathered crystals similar to those of cocaine. *Following* this crystallization, in solutions down to 64 a yellow amorphous precipitate forms, and from this form gradually dark round crystals or dark rosettes that are aggregates of grains. The test with a minimum of reagent is sensitive to about 1:60, while the dark rosettes are obtained down to about 1:125.

*Palladium Chloride.* Sphero-crystals form. They may become rosettes of thin rods. Sensitive to solution 32 (about 1:250).

*Picric acid.* Large branching splinter crystals and curved branching crystals form slowly from the amorphous precipitate in concentrated solutions, or on stirring. Crystals can be obtained down to solution 8, or 1:1000, but as with cocaine crystallization is somewhat uncertain.

*Na Picrate.* Readier crystallization than with the acid. Fern-like rosettes form slowly; or with stirring there is complete crystallization, mainly in fern rosettes, with some long irregular yellow plates. Sensitive to solution 32 (about 1:250).

*Trinitroresorcin.* Crystallizes readily and completely, with three kinds of crystals in the same solution; good-sized needles in rosettes, yellow "smudge rosettes" (smaller), and quite small grain-platelets. Microscopically all the crystals are yellow. Sensitive to solution 64 (1:125).

*Potassium Dichromate.* The precipitate crystallizes slowly, or on stirring, in large thick grain-sticks, orange.

*Gold Cyanide.* The precipitate soon crystallizes completely and densely in fern-like plates. With stirring crystals are obtained down to solution 16, about 1:500.

*Mercuric Na Chloro-Nitrite.* With stirring, the most concentrated solution gave partial crystallization in colorless transparent prisms. Both Mercuric Nitrite reagents give white precipitates that soon turn yellow—a color test.

## Cocaine—General Properties

1. Cocaine is methyl-benzoyl-ecgonine. It is usually sold and used in the form of the hydrochloride.

appearance of which has given cocaine the nickname "snow". Free cocaine is a white crystalline solid.

2. Appearance. The hydrochloride (although it also occurs as large crystals) is usually in the form of glistening white flakes, the

3. Solubility. The hydrochloride is very soluble in water. Adulteration by such substances as phenacetin or acetanilid is at once observed by their failure to dissolve readily. The free base is insoluble in water but dissolves readily in dilute acids, and is soluble in the common organic solvents and in petroleum ether.

4. Odor on solution. Cocaine hydrochloride on dissolving in water gives off a pleasant odor, slight but distinct. This test is not mentioned by any of the authorities, so far as I know. A narcotic agent called it to my attention.

5. Physiological effect. Applied to the tongue it causes tingling and numbness, and a curious smooth feeling of the anaesthetized part. Mulliken gives specific directions for the test.[4]

6. Extraction. Cocaine is not removed from acid solution by immiscible solvents but is readily extracted from basic solution. Carbonate or ammonia should be used, never strong alkali, or the cocaine will be hydrolized. Extraction with petroleum ether will separate it from many alkaloids.

7. Melting point and volatility. Free cocaine melts at less than the boiling point of water (at 98 degrees, according to Mulliken); and enough will sublime between two watch-glasses on the water bath for detection with gold chloride.

8. Hydrolysis. Cocaine is hydrolized very readily by alkali on heating. Methyl alcohol, the benzoate of the alkali, and ecgonine, are formed. Concentrated acids will also cause hydrolysis, forming methyl ester of the acid, benzoic acid, and a salt of ecgonine. Cocaine must not be warmed or let stand in alkaline solution or there will be little or no cocaine left as such.

### Direct Chemical Tests (aside from microscopic tests)

1. Color tests. None of any value, except insofar as the four tests following can be called color tests. Most reagents for color reactions (Froehde's and Marquis' reagents, etc.) give no color at all with cocaine. Concentrated nitric acid is perhaps the most convenient reagent for discovering admixture or adulteration by a color test.

2. Potassium permanganate retains its purple color in acidified cocaine solution. Those adulterants or substitutes that are reducing agents discharge the color.

3. Mercurous nitrate solution, used to moisten the solid hydrochloride, yields a dark gray. The reagent used was made with concd. $HNO_3$—10 cc. water—90 cc. mercury in excess. This is a far bet-

(4) Mulliken: Identification of Pure Organic Compounds.

ter form of the test than triturating the cocaine hydrochloride with calomel and moistening with 90 per cent. alcohol, as is directed by several text-books. Novocaine hydrochloride gives the same test. (This is really a reagent test, depending on the formation of metallic mercury, while the two preceding are negative tests. Strictly only the following tests are direct chemical tests for cocaine.)

4. Phosphotungstic acid, added to the solution on the spot-plate, gives a pure white precipitate. Numerous other alkaloids do likewise, but many, including novocaine, give precipitates tinted pink, salmon, orange, or yellow. A 10 per cent. solution of phosphotungstic acid, not containing any nitric acid, is used.

5. Cobalt sodium thiocyanate gives a blue precipitate from acidified solution. Although actually a precipitation test, this has the effect of a color test as the reagent solution is pink. The best method for the test, I think, is to dissolve a convenient quantity of the sample, on the spot-plate, in one drop of diluted sulfuric acid (1+3), and add one drop of cobalt sodium thiocyanate solution. Cocaine gives a blue precipitate. From neutral solution novocaine also gives a blue precipitate, but with the acid its solution will remain clear and will simply be colored pink by the reagent. There are, to be sure, many alkaloids that behave like cocaine in this test. A test of this nature was originally given by Mr. Young of the Washington laboratory of the Industrial Alcohol Bureau.[5]

6. Sticking test. Wagner's reagent, and picric acid, applied to the solution on the spot-plate, yield heavy precipitates which form a varnish-like coating on the plate, and stick so tightly that they cannot be cleaned off by washing and rubbing with a towel. (The picric acid precipitate however may crystallize on standing.) Novocaine gives the same test. An alkali, or mineral acid, or alcohol, will clean the plate.

7. Borax test. When a drop of 0.5 per cent. borax solution is added to some solid cocaine hydrochloride (best on the microscope slide) solution is immediately followed by the formation of a white precipitate which soon crystallizes, generally in rods. This test is due to Mr. Ryan of the Washington laboratory of the Industrial Alcohol Bureau.

## Derivative Tests

1. Benzoic acid. Add NaOH in excess to a cocaine solution, and heat. Add some alcohol, if necessary to hold the cocaine in solution until hydrolyzed, and later evaporate it off. Hydrolysis is complete when an acidified drop of aqueous solution gives no precipitate with gold chloride. On acidifying the hydrolyzed solution benzoic acid is set free. It is not very soluble in cold water and will be precipitated if the solution is at all concentrated. It can be detected

(5) James L. Young, in *Am. Jour. Pharm.*, 103, 709 (1931). *C. A.*, 26, 1063.

even though very little cocaine was present by shaking out the acid solution with ether. The ether is separated and shaken with dilute ammonia, which is then evaporated to dryness on the water bath. The ammonium benzoate is then taken up in a little water and a drop or two of nearly neutral ferric chloride solution added. A flesh colored precipitate of ferric benzoate results.

Vitali's test gives an odor test for the benzoyl group. Dissolve the cocaine in concentrated nitric acid on a watch-glass, evaporate to dryness on the water bath, cool and add alcoholic KOH. The odor of ethyl benzoate can then be noted, but it disappears quickly if the quantity of cocaine was small.

A simpler procedure is to dissolve the cocaine in a little alcoholic KOH, warm, and pour into a few cc. of water, and note the odor of ethyl benzoate.

2. Ecgonine. This is the most important and characteristic product of the hydrolysis of cocaine, and is the basic or amine part. When the benzoic acid is extracted by ether from the acidified solution the ecgonine remains in the water, in which it is quite soluble. (In fact, it cannot be extracted from aqueous solution.) It is readily identified by its precipitates from dilute acid solution with various alkaloidal reagents. The best tests are probably those with Dragendorff's reagent and gold bromide. Dragendorff's reagent (preferably the double-strength form) gives two different types of crystals, depending on the temperature. One type, formed on the hotter days, or in warm solution, consists of large orange plates which when separate and perfect are octagonal. The other type consists either of orange-red hexagonal plates, or dark red six-pointed stars. Gold bromide (brom-auric acid) gives red square platelets, generally pretty small.

(*To be continued*)

# STUDIES IN PERCOLATION*

## III

By Milton Wruble

(*Continued from the June Issue.*)

### 2. Romershausen's "Luft"- and "Dampf-Presse"

As has been shown, Réal's "filtre-presse" represents an adaptation of the pressure filter [1] to Dubelloy's *cafetière*.[2] Originally intended, in part at least, for the extraction of ground coffee with water, the pressure was attained by means of a column of water. Inasmuch as pressure was regarded as of the essence of the apparatus, the higher the column the more perfect the extraction. However, the height of the water column proved a practical inconvenience. Hence, a column of mercury, the density of which is 13.6 times greater than that of water, was substituted.[3] While this substitution enabled a greater compactness of the apparatus, the increased pressure thus made possible, necessitated a corresponding strengthening thereof. Moreover, the inconvenience of the spilling of mercury because of insufficiently tight joints had to be taken into consideration. The application of the apparatus to pharmaceutical extractions with alcohol in no way lessened the difficulties and inconveniences encountered when Réal's press was introduced into the apothecary's laboratory.

Apparently it was Kastner, who appears to have been interested in apparatus producing air pressure, and who suggested, as early as 1818, that a "Luftpresse" might supply the pressure as well as a column of water or mercury.[4] It was Romershausen who acted upon the suggestion, had his apparatus patented and described them in a pamphlet published in 1818.[5] Judging from the attention given the new apparatus in contemporary pharmaceutical literature, the modification was well received. Marechaux, in 1821, refers to the supposed improvement in the following words:

"Gewoehnlich gelangt der Geist auf Irrwegen zum Ziel, das Einfachste findet er zuletzt. Wie leicht war es nicht, das lange Rohr der Realschen Presse zu verkuerzen, und vermittelst eines Drukkolbens, was schon mit allen hydraulischen Pressen geschah, denselben Zweck zu erreichen, den man vermittelst Queksilber, oder

*Madison Pharmaceutical Experiment Station.

Luftcompressions-Apparate zu bewerkstelligen suchte. Dem Doktor Rommershausen blieb das Verdienst vorbehalten, die einzige Einrichtung vorzuschlagen, welche geeignet seyn konnte die Realsche Presse ins Leben einzufuehren." [6]

In the numerous modifications of his apparatus, Romershausen applied pressure in three different ways:

1. By compressing the air above the menstruum, thus forcing it through the comminuted material.

2. By creating partial vacuum in the receiver, thus sucking the menstruum through the comminuted material.

3. By forcing steam through the material to be extracted.

His apparatus were manufactured for use in the brewing, tanning, dyeing and pharmaceutical industries.

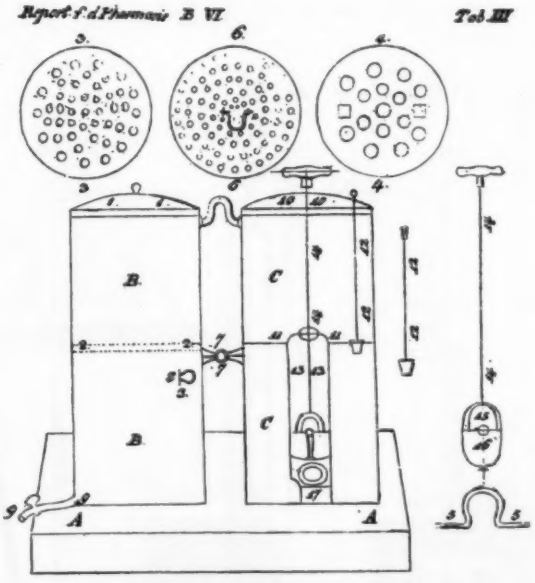


**Fig. 1—ROMERSHAUSEN'S AIR PRESS.**

**The two tin cylinders B and C are mounted on the support A, and are provided with the covers 1 and 10. On the support the diaphragm 3 is placed, covered with a straining cloth which is held in position by the diaphragm 4, which in turn is fastened by the clasp 5. A third diaphragm 6 is used to cover the substance to be extracted. The two cylinders are united by the tube 7 provided with a stopcock. The lower part of B is also provided with a stopper at 8 in order to allow the percolate to flow out at 9. The lower section of C is converted into an airtight compartment by the cover 11, which is provided with an opening and stopper at 12. The parts indicated by 13, 14, 15, 16 and 17, belong to the suction pump necessary to create a vacuum.**

Inasmuch as Romershausen's original pamphlet is not available, we are dependent for our information on articles in pharmaceutical and other journals based on this publication.

During the same year in which Romershausen published his pamphlet, Trommsdorff called attention to Romershausen's improvements of the Réal press, but gives no illustrations of the apparatus.[7] In the same year Buchner also gave a brief account of the improvement, but does not illustrate the device.[8]

A third account is that by Kastner,[9] who classifies Romershausen's "Luftpressen" into three groups, viz.:

1. Those intended for domestic use (coffee, etc.).
2. Those intended for apothecaries, which he designated "Tincturmaschinen" and constructed of five sizes.
3. More elegant apparatus for "the coffee and tea table."

The first illustrated journal article appears to be that by Buchner of the same year.[10]

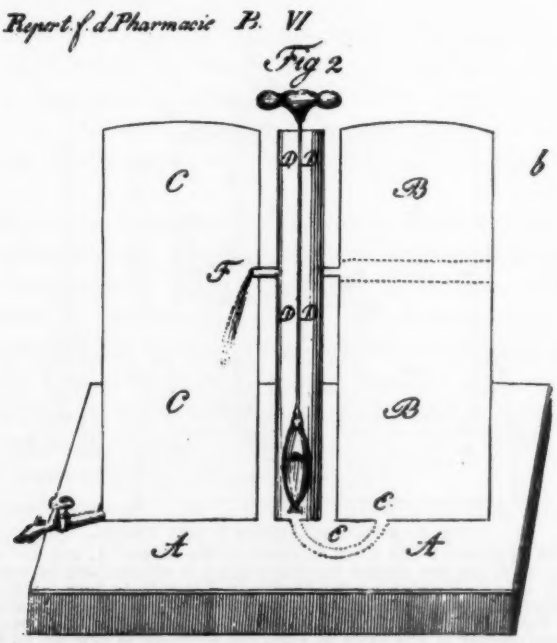


**Fig. 2—ROMERSHAUSEN'S MODIFIED AIR PRESS.**
**The suction pump is outside of the cylinder and the percolate is not allowed to collect underneath the percolator B, but is at once pumped into the reservoir C.**

In the same year, Romershausen, in a letter to Trommsdorff, discusses pressure percolation as carried out by means of his apparatus and points out its adaptation to pharmaceutical practice.[11]

In 1822 Romershausen published a historical account of extraction presses.[12] While some of his contemporaries praised his improvements over the Réal apparatus, Parrot concluded after a number of experiments that pressure extraction was unnecessary and that ordinary extraction with the aid of a screw press was just as effective provided that the material to be extracted was first soaked with the menstruum and allowed to stand prior to expression.[13] To this Romershausen took exception claiming that Parrot's interpretation of the experimental results were faulty; also, that if he had used Romershausen's press he would not have reached his conclusions.[14]

It has been pointed out that Romershausen manufactured a number of styles and modifications of his air press. Of modifications by others, that by Beindorf was given publicity in the pharmaceutical press.

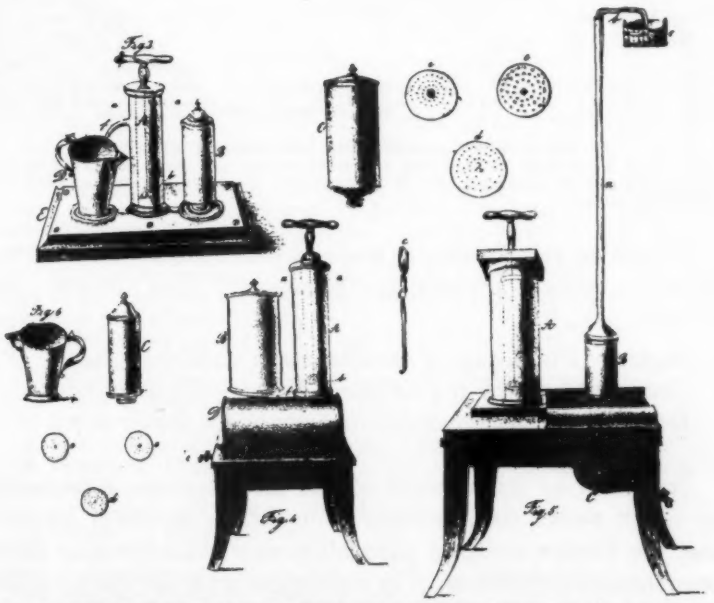

**Fig. 3—BEINDORF'S MODIFICATION OF ROMERSHAUSEN'S AIR PRESS.[15]**
**Figs. 3 and 4—Simpler and more compact types.**
**Fig. 5—This apparatus is supplied with an extra supply of menstruum in vessel c.**
**Fig. 6—A graduate for measuring liquids.**

All of the apparatus described are provided with suction pumps creating a partial vacuum underneath the powder to be extracted, thus producing atmospheric pressure from above. Romershausen's first method of applying pressure from above does not appear to have received consideration in the apparatus described in pharmaceutical and other scientific journals. His third method found application in his "Dampfpresse." Apparatus of this type were described by Marechaux. One of these is herewith reproduced.[16]

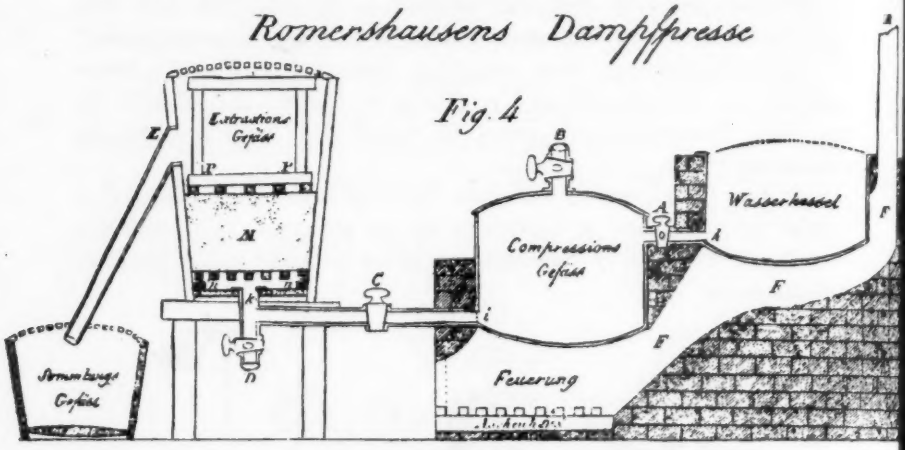


**Fig. 4—ROMERSHAUSEN'S "DAMPFPRESSE".[16]**
**The water warmed in the reservoir, is heated so that the steam generated will force it upward through the material "M" to be extracted, the extract to be collected in the "Sammlungs-gefaess".**

In closing this survey, it may be pointed out that Beindorf's suggestions received attention in contemporary texts and even somewhat later, viz., in

Buchner, *Einleitung in die Pharmacie* (1822), p. 247.
Geiger, *Handbuch f. Pharmacie,* Bd. I (1830), p. 141.
Doebereiner, *Deutsches Apothekerbuch I* (1842), p. 79.

Imperfect as this account of the second phase of percolators may be, it shows that, as interest in Réal's invention seemed to wane, the further study of percolation received a stimulus through Romershausen's inventions. In connection with the story of Réal's apparatus and modifications thereof by others, it has been pointed out that the subject of percolation entered a new phase when the Boullays, *père et fils,* developed the process without pressure. In

this connection, attention should once more be directed to the claim made by Professor Parrot of Dorpat as early as 1823, viz., that pressure applied in the percolator was unnecessary, indeed that a special percolator was uncalled for since, by proper treatment, the same results could be obtained by using an ordinary screw press. This criticism, however, leaves out of consideration the phase of displacement which is so important in the process of percolation. Hence, when the excitement of novelty due to Romershausen's inventions was over, the idea of pressure percolation appears to have been abandoned for a time, at least so far as pharmaceutical operations are concerned.

## REFERENCES


1. See Réal's "Filtre-presse" and its "Modifications," footnote 2, this journal, p. 290. See also Cadet: "Les Anglais ont fait une application de cet principe à la purification des huiles." *Journ. de Pharm.* 8 (1816), p. 165.
2. Dubelloy's *cafetière.*
3. Column of mercury first proposed by Réal (*Journ. de Pharm.* 8 (1816), p. 166), was later applied by Trommsdorff (*Journ. der Pharm.* 25, II (1816), p. 47).
4. *Berl. Jahrb. f. d. Pharm.* 20 (1819), p. 392. Kastner's original suggestion was made in the *Deutscher Gewerbsfreund,* 1818, edited by him. Unfortunately, this journal is not available. Hence Prof Kastner's words may here be quoted: "Im ersten Hefte des dritten Bandes . . . meines D. Gewerbsfreundes machte ich auf eine frueherhin schon von mir in Vorschlag gebrachte . . . Extractions-Saugpumpe . . . und ueberhaupt auf die Anwendung der Luftpumpen Einrichtung auf verschiedene Gewerbe aufmerksam . . .; nach einiger Zeit meldete mir Herr Dr. Romershausen zu Acken an der Elbe, dass er jene Vorschlaege weiter verfolge, und bald darauf erfand er die nach ihm benannte Luftpresse. . . ."
5. "Dr. Romershausen's Luftpresse, eine in den Koeniglich-Preussischen Staaten patentirte Maschine zum Extrahiren, Filtriren, und Destilliren. 18 Heft, die Beschreibung und allgemeine Anleitung zum Gebrauch dieser Vorrichtung nebst einigen Andeutungen zur vortheilhaften Anwendung derselben in der Haushaltung enthaltend." Zerbst., bei A. Fuechsel. 1818. Unfortunately a copy of this pamphlet has not yet been located. However, references to it may be found in the following journals:—
   *Buchners Repert. f. d. Pharmacie* 6 (1819), p. 317.
   *Berl. Jahrb. f. d. Pharm.* 20 (1819), p. 396.
   Buchner's *Anleitung in die Pharmacie,* 2ten Aufl., p. 252.
   *Ann. d. Physik* 77 (1824), p. 294.
6. *Dinglers Polyt. Journ.* 5 (1821), p. 402.
7. *Neues Journ. d. Pharm.* 2 (St. 2), (1818), p. 539.
8. *Repert. d. Pharm.* 4 (1818), p. 406. This originally appeared in the *Literatur-Zeitung* for 1818, No. 28.
9. *Berl. Jahrb. f. d. Pharm.* 20 (1819), p. 392.
10. *Repert. d. Pharm.* 6 (1819), p. 316.
11. *Neues Journ. d. Pharm.* 3, I (1819), p. 453.
12. *Schweigger's Journ. f. Chem. u. Phys.* 34 (1822), p. 106.
13. *Ann. der Physik* 75 (1823), p. 423.
14. *Ibid.* 77 (1824), p. 291.
15. *Mag. f. d. Pharm.* 9 (1825), p. 176.
16. *Dingler Polyt. Journ.* 4 (1821), p. 420.

### 3. The Contributions of the Boullays, père et fils

As pointed out in the introductory remarks, it is not quite true that the process of percolation "never became popular in France," as it is erroneous to claim that it "was ignored in Germany." That it was not ignored in Germany has been fully demonstrated in the previous chapters. The justification for the erroneous statement may be found in the fact that percolation, as we think of it in this country, was not practiced in Germany for a long time after we had adopted and developed it. Its development in this country, however, is not based on the pressure percolation idea so enthusiastically pursued for a brief period in Germany, but on the non-pressure percolation practice developed by the Boullays, *père et fils*. It was through their experimentation and the reports of their experimental results that the attention of the American pharmacist was drawn to this process. To anyone at all acquainted with American pharmaceutical literature of that period this is not surprising. So far as there was any American pharmaceutical literature during the first half of the nineteenth century, this was based largely on English literature. Next came French pharmaceutical literature. One has but to page the earlier volumes of the *American Journal of Pharmacy* to appreciate the general accuracy of this statement. It was not until Maisch became editor of the journal that German literature received due recognition. By this time, however, the German apothecaries had dropped pressure percolation and had returned to the older processes of maceration and expression.

To the American student, the work of the Boullays is of twofold interest. Firstly, it was they who demonstrated the uselessness of pressure, no matter what the mode of application, and thus removed the unnecessary difficulties that accompanied the operation of Réal's process and its modification by Romershausen. Secondly, it was through the reports of the Frenchmen that they became interested in the process even if they may have known vaguely of the earlier apparatus and their uses and difficulties. Of this, however, there appears to be no evidence thus far.

The communications of the Boullays are recorded in three papers. The first of these appeared in 1833 and was read before the *Société de Pharmacie*.[1] In this paper they gave due credit to earlier workers, including Réal. They pointed out, however, the disadvantages of the long column of mercury in the Réal press and

the difficulty of producing tight joints due to the pressure, which to their minds was unnecessary. In this paper they introduced the phrase, *procédé par déplacement.*

Later in the same year they published their second report in which they gave a very comprehensive treatment of their so-called *méthode de déplacement.*[2] Once more they emphasized that the high column of water proposed by Réal had no other effect than to render the apparatus less applicable and that the Réal apparatus minus the pressure was nothing more than the *cafetière de Dubelloy,* known for a long time.

The last of these reports was published in 1835.[3] This included experimental results on new drugs and, the results of several contemporary workers, among them Buchner, DuBlanc, Soubeiran and others. For the first time several types of percolators were described.

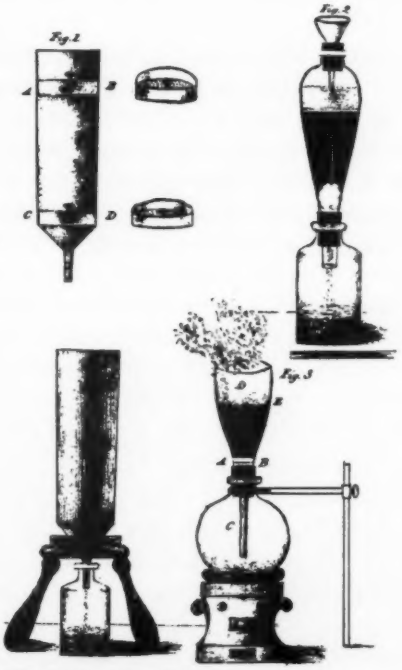

**Fig. 1—Percolators described by the Boullays.**
**A B and C D are removable perforated plates.**
**Fig. 2—Donovan's apparatus for filtering out of contact with air.**
**Fig. 3—A small apparatus for hot extraction (cafetière).**

That these papers stirred up much discussion and interest is evidenced by the publications in the French and German journals of the day. While one of their countrymen, Simonin, lauded their work in the following manner: "Je ne puis terminer sans rendre hommage à MM. Boullay. Leur procède si simple est applicable à tant d'operations, qu'il doit produire une veritable révolution en pharmacie;" [4] Geiger, in Germany, stated in a comment following an abstract of their first paper in the *Annalen der Pharmacie*—"Was hier ueber die Wirkung der Realschen Presse geaeussert wurde, ist in Deutschland laengst bekannt, und ich habe mich schon vor 17 Jahren in den Schriften: 'Beschreibung der Realschen Aufloesungs-Presse u. s. w. Heidelberg 1817,' so wie in meinem *Handbuche der Pharmacie,* dahin ausgesprochen, dass sie ein vollkommenes Auswaschen (Erschoepfen) der Faser mit der geringsten Menge Extractionsfluessigkeit sey. Dass uebrigens die Realsche Presse unnuetz sey und ein Trichter dieselbe ersetzen koenne, glaube ich nicht." [5]

Much argument as to priority also arose at this time. Robiquet, a contemporary of the Boullays, stated at a meeting of the Pharmaceutical Society of Paris that a similar apparatus had been used at the Paris School of Pharmacy "for a long time." [6]

A year later this same investigator described an apparatus [7] to which he had previously referred [8] and which he had successfully employed in the extraction of bitter almonds.


**Fig. 4—Robiquet's Apparatus.**

The Boullays answered [9] Robiquet's charges and refuted in no uncertain terms his false accusations. They made it clear that their only claims were the application of a new method to a very large number of medicinal substances which are otherwise altered more or less by prolonged evaporation.

A further reply by Robiquet [10] stated that the Boullays had no reason to claim priority for the invention, inasmuch as he had used the same process for a number of years in his private laboratory, in his factory, and at the Paris School of Pharmacy. He also stated at this time that he had his apparatus made for him in accordance with his own specifications by M. Alcoque and that many pharmacists had asked for it under the name of "the apparatus of Robiquet."

Guibourt, another contemporary Frenchman, gave credit to Payen for having developed the process prior to the work of the Boullays. He expressed himself in the following manner [11]—"Secondement j'ai à me réprocher de n'avoir pas cité M. Payen comme l'un des premiers qui aient montré l'application que l'on pouvait faire de la méthode de déplacement à la pharmacie."

Guilliermond, however, gave due credit to the Boullays for their work. In a thesis presented to the *École de Pharmacie de Paris,* in 1835, in which he carefully traced the development of percolation, he stated, after crediting the earlier workers for their efforts, "Mais il appertenait à MM. Boullay père et fils de faire de ce procédé une application plus étendue, soit en étudiant le phénomène d'une manière générale dans la théorie, soit en donnant de nombreux exemples de son application aux préparations pharmaceutiques, soit enfin en provoquant et en appelant sur ce point l'attention et les recherches des pharmaciens observateurs." [12]

The work of the Boullays soon began to attract attention in the United States and Duhamel, who was the first American to write on percolation, stated "But to Messrs. Boullay belongs the honor of having established what was before a mere hypothesis. By their researches they not only proved that it admitted of very extensive application, but by furnishing practical results in some new and efficient preparations they demonstrated it to be of the highest utility in pharmacy." [13]

There is no doubt then that the Boullays should be credited with their contribution to the evolution of pharmaceutical percolators and as evidence that their work was not soon forgotten, numerous

French references to this appear in the journals as late as the sixties when the much discussed question before the Committee of Revision of the United States Pharmacopœia was whether to make maceration or percolation the official process for the preparation of tinctures and fluidextracts.[14]

REFERENCES

1. *Jour. de Pharm.* 25 (1833), p. 281.
2. *Ibid.* 25 (1833), p. 393.
3. *Ibid.* 27 (1835), p. 1.
4. *Ibid.* 26 (1834), p. 109.
5. *Annalen der Pharm.* 7 (1833), p. 318.
6. *Jour. de Pharm.* 25 (1833), p. 322.
7. *Ibid.* 26 (1834), p. 79.
8. Robiquet and Boutron had published two papers in 1830 and 1831 describing in each case the use of a percolator in the extraction of bitter almonds and mustard seeds. *Annales de Chim. et Phys.* 44 (1830), p. 352; and *Jour. de Pharm.* 23 (1831), p. 279.
9. *Jour. de Pharm.* 27 (1835), p. 188.
10. *Ibid.* 27 (1835), p. 113.
11. *Jour. de Chim. Méd.* 1 (ser. 2), (1835), p. 225.
12. *Jour. de Pharm.* 27 (1835), p. 349 (abstract by Cap).
13. *Am. Jour. Pharm.* 10 (1838), p. 1.
14. *Jour. de Pharm.* 74 (1862), pp. 60, 116, 257, 264. *Ibid.* 75 (1862), p. 196.

### 4. Early Developments in the United States

It has already been pointed out that interest in the new process by American pharmacists was aroused by the publications of the Boullays which became known in this country. So enthusiastic the pharmacists of the United States became that in their enthusiasm they were inclined to overlook what had been going on in European countries and was still going on. As a result they regarded the process as a typically American development, though its invention was ascribed to a Frenchman. How even modern writers on the subject have overlooked the shortlived but enthusiastic development of pressure percolation in Germany has been indicated. This was due, no doubt, to the fact that publications in German journals were unknown to American writers. It remains to be pointed out that they appear to have been equally unaware of the early pharmaceutical progress made in English speaking countries. Thus the editor of the American Druggist and Pharmaceutical Record in 1897 [1] claimed that it was the U. S. Pharmacopœia of 1840 (which did not appear until 1842) which first made the process official. To this the editor of the *Chemist and Druggist* [2] replies by pointing out that the Edin-

burgh Pharmacopœia of 1839 not only made the process official but enumerated a long list of tinctures, etc., which could be made advantageously in accordance therewith. He also points out that the process was being used extensively in England at that time.

If, as Americans, we should be ever ready to give credit to our German and British confreres, we need not hesitate to point with satisfaction to the improvements made by our fellow pharmacists in connection with a process which, according to Tschirch, is the only improvement made in extraction during the past century.[3]

The first communication on the subject which appears to have appeared in an American publication [4] is a reprint by Soubeiran which had been contributed originally to a French journal [5] in 1836. In it the author reviews the work done by the Boullays, Robiquet, Guillermond and others, stating that the most important information is to be found in the publications of Guillermond [6] and that the best apparatus have been described by the Boullays.[7] Two years later the first article from the pen of an American pharmacist appeared. It is that of the Philadelphia pharmacist Duhamel.[8] Tracing the history of the process back to Réal and stressing the contributions made by the Boullays, he records the results of some of his own experiments.[9] A second paper by Duhamel and Procter [10] appeared a year later.[11] They state that while "in France this method has been extensively applied, in this country it is hardly known, much less applied." The process had been made official in the French Codex of 1835. They make a plea for its introduction into the next Pharmacopœia. This step was taken, but with the following precautionary advice by the medical revisers of the U. S. P.: "And it is strongly recommended to those who have not made themselves practically familiar with the various sources of error in the method of displacement, to postpone its application whenever an alternative is given in this work until they have acquired the requisite skill." [12]

With the introduction of fluidextracts into the U. S. P. of 1850, to be made by the process of percolation, a special impetus was given to the study of this process and of improvements thereon. Thus Grahame [13] concludes an article in which he reviews the history of the process, the theoretical aspects underlying it, also his own experiences therewith, with the following words: ". . . the great advantages of the displacement process, as thus conducted, consist in the facility it affords of obtaining very concentrated solutions of vegetable substances in a comparatively short period of time."[14]

In the same year Squibb [15] published his first article on the subject in which he describes and illustrates two types of percolators, viz., his automatic percolator and his well-tube percolator.[16] When, after the Civil War, alcohol became high priced because of an internal revenue tax of many times the cost of production, he developed the process of repercolation.[17] Squibb's work on the subject has been so extensive and important that it will be considered in a chapter by itself.

This brief chapter on the early development of percolation in the United States would be incomplete without reference to the work of such men as Diehl and Lloyd. Possibly that of Rother, Oldberg and others should also be mentioned. In closing this aspect of our subject it may be proper to point out once more how ingrained the idea had become that percolation was essentially an American process. For this purpose a paragraph from a paper by Lloyd in 1879 may be quoted: "Virtually percolation had been employed for ages with civilized and even partly barbarous nations, as for example, in the making of saltpetre and potash. Yet while the idea was not new, its application to the preparation of tinctures and fluidextracts was original, as far as I can learn, and thus we are indebted to Professor Procter as though the principle for separating soluble from insoluble matters was new in the world's history." [18]

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1. Vol. 30, pp. 164 and 283.
2. Vol. 50 (1897), p. 922.
3. Fédération Internationale Pharmaceutique, Lausanne, 1925. Translated and printed by the *Pharm. Journ.*, vol. 115, p. 362; copied by the *Am. Dr. & Ph. Rec.* 73, Dec. 1925, p. 19.
4. *Am. Journ. Pharm.* 8 (1836), p. 221.
5. *Bull. Gén. de Thérap.* 9 (1836), p. 349.
6. Thesis presented to the *École de Pharm. de Paris;* abstract by Cap in *Journ. de Pharm.* 27 (1835), p. 349.
7. *Journ. de Pharm.* 27 (1835), p. 1.
8. For a biographical sketch, see J. W. England, "First Century of the P. C. P.," p. 373.
9. *Am. Journ. Pharm.* 10 (1838), p. 1.
10. *Ibid.* 11 (1839), p. 189.
11. For a biographical sketch, see J. W. England, *l. c.*, p. 124.
12. U. S. P. 1840, p. XXII.
13. For a biographical sketch, see J. W. England, *l. c.*, p. 115.
14. *Proc. A. Ph. A.* 7 (1858), p. 294.
15. For a biographical sketch, see J. W. England, *l. c.*, p. 216.
16. *Am. Journ. Pharm.* 30 (1858), p. 97.
17. *Proc. A. Ph. A.* 15 (1867), p. 391.
18. *Ibid.* 27 (1879), p. 691.

## THE ONE HUNDRED AND ELEVENTH ANNUAL COMMENCEMENT OF THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE

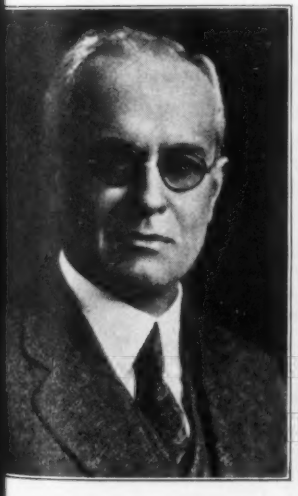
THE One Hundred and Eleventh Annual Commencement was held in the College Auditorium at 8 P. M., June 7, in the presence of a large audience.

The invocation was pronounced by the Reverend Father Joseph A. McDonald, rector of the Church of Our Mother of Sorrows. The candidates for graduation were presented to President Wilmer Krusen by Dean of Pharmacy, Charles H. LaWall and by Dean of Science, Julius W. Sturmer. Degrees in course in pharmacy, chemistry, bacteriology and pharmacognosy were conferred upon 161 students.

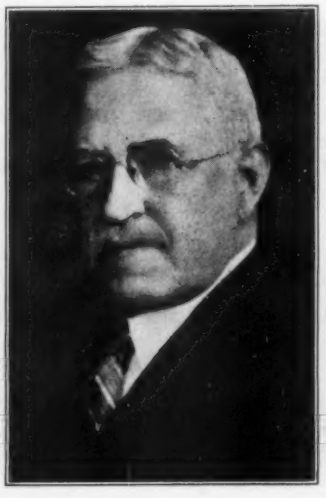
In addition, the degrees of master in pharmacy *honoris causa* were received by the following:

Dr. Theodore J. Bradley, distinguished pharmacist, chemist and educator, who has served twenty-one years as dean of the Massachusetts College of Pharmacy in Boston.

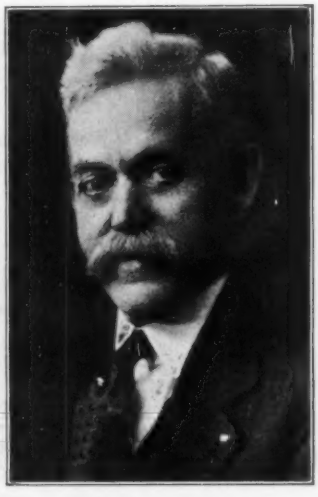
Henry K. Mulford, 1887, graduate of this College, founder and long the directing head of the H. K. Mulford Company, pioneer producers of vaccines and serums and now director of the biological



Theodore J. Bradley



Henry K. Mulford



Jacob L. Nebinger

and research laboratories of the National Drug Company, and president of the Mulford Colloid Laboratories.

Jacob L. Nebinger, 1885, graduate of this College, for twenty-four years in charge of the prescription department of the Philadelphia drug store founded by the late William H. Llewellyn, 1877, and now a member of the teaching staff of the College.

An orchestra composed of West Philadelphia high school students, under the direction of Harry P. Hoffmeister, assistant professor of German at the College, presented a musical program during the ceremonies.

The address to the graduates was delivered by Dr. George Earle Raiguel, physician, author and traveler, following which President Krusen gave a farewell message to the graduating classes. Degrees in course, certificates and prizes were awarded as follows:

MASTER IN PHARMACY (Honoris Causa)

Theodore J. Bradley — Henry K. Mulford
Jacob L. Nebinger

DOCTOR IN PHARMACY

Herbert Bohn

MASTER OF SCIENCE IN CHEMISTRY

Joseph C. Haefelin — Allen F. Peters
Amelia M. de Ponce

MASTER OF SCIENCE IN PHARMACY

Kurt E. Steiger

MASTER OF SCIENCE IN BACTERIOLOGY

Jeanne D. Dreier — John N. McDonnell

BACHELOR OF SCIENCE IN CHEMISTRY

Albert Bloom — Richard E. Houghton
Stephen F. Colalongo — Edward A. Listokin
Lane V. Collins, Jr. — Wilbur B. Millington
Walter L. Nelson

BACHELOR OF SCIENCE IN BACTERIOLOGY

Joseph H. Kelly — Werner W. W. Ruthenberg

BACHELOR OF SCIENCE IN PHARMACY

Elizabeth C. Adams — James Q. Mackey
Harrison R. Boggs — Saul Malasky
William L. Byrnes — Abraham Marcus
Abraham Cohen — Sigmund Moerman
Rubin Greenberg — Louise A. Moffses
Francis P. Kelly, Jr. — Margaret A. Morgenthaler
Guido Lorenzoni — Mary B. O'Connor

George A. Panarello
Estelle A. Pavilonis
Samuel A. Rosenbaum
Joseph R. Santoro
Michael M. Selector
Linwood F. Tice

PHARMACEUTICAL CHEMIST

Albert J. Feicht, Jr.
Bernard Protigal

GRADUATE IN PHARMACY

Llewellyn S. Adelman
Frances R. Allone
Esther N. Altshuler
William F. Andiario
Edward N. Arshan
Edgar C. Bekes
Wallace S. Bell
Charles W. Bennett, Jr.
Julius Bernstein
Richard L. Boaman
Harry H. Bock
Joseph M. Boltz
Martin R. Bower, Jr.
Adelaide H. Brandt
William J. Braude
Francis J. Brocani
Milton J. Brown
John M. J. Burns
Mary Cammarota
Edward R. Carl
Vincent C. Cartusciello
Nathan Cohen
Carmelo J. Coletta
John A. Dereskevich
August Di Riego
William G. Dreibelbis
Miriam C. Dubin
Eugene C. Dunham
Charles Eckstein
David N. Ellis
Frederick Else, Jr.
Frank C. Falchek
Harry J. Feather
Natalie R. Feldman
William Ginzburg
Cecil J. P. Gray
Frank A. Groblewski, Jr.
Woodrow W. Groff
Harold M. Gruber
Jerome F. Haaz
Harold R. Hafer
Orville Hann
Edmund V. Havira
Richard H. Herbine
Samuel Herman
Elmer C. Hillman
William M. Holsberg
Herman G. Hornung
Solomon Isserman
Michael Javoronok
George D. Jenkins
Hiram E. Keefer
Joseph P. Kelly
Martin Kirshenbaum
Bernard B. Kline
Ralph L. Kline
Isryl M. Krause
Walter J. Kropp
Robert H. Lentz
Harry A. Levenson
Harry H. Levin
Louis S. Lyon
Claude E. Markley
Charles R. Mattei
Anthony J. Mazzucca
Ralph D. McKinstry
Russell A. Miller
Nathan Mirman
Emanuel H. Modeck
William L. Morrison
Joseph Ness
William E. Ogden
Edward Oxman
Benjamin Parson
Ray T. Peffer
Maxwell S. Perlstein
Margaret M. Petruno
Charles R. Pimlott
Claude P. Pinkerton
Edmund M. Points
Fred P. Ragains
Harry W. Rementer, Jr.

Robert M. Reynolds
Herman J. Rocconi
Sidney D. Rosenfeld
Isadore Rosenthal
Cyril A. Sakalosky
Reynold L. Salvatore
William L. Scharadin
Arthur Scott
David P. Secon
David M. Sherrick, Jr.
Thomas D. Simmons
Edward J. Smith
Narcey A. Stapinski
Donald B. Stegner
John J. Stepanik
Marlin B. Stetler
William W. Stinson
John R. Stout
Samuel F. Tancredi
Howard F. Watson
Albert J. Windfelder
Joseph A. Yantoshik
Jacob Zalesky
Walter J. Zukoski

CANDIDATES WHO HAVE COMPLETED SPECIAL COURSES AND HAVE QUALIFIED FOR CERTIFICATES

(This does not include students who completed courses in these subjects for credits for a degree.)

CERTIFICATES IN BACTERIOLOGY

Seymour Halbert
Thomas W. D. Harrison
Lory C. McAllister
Joseph A. Montalbano
Joseph M. Muniz
Marie A. Reilly
Sol Sherson

CERTIFICATES IN CLINICAL CHEMISTRY

Harry J. Bailen
Cecil J. P. Gray
Seymour Halbert
Thomas W. D. Harrison
Lory C. McAllister
George A. Miller
Joseph M. Muniz
Marie Anne Reilly
Sol Sherson
Genevieve D. Slaughter

## Award of Prizes 1933

GRADUATES IN PHARMACY

Designated as "Distinguished"

With General Average Over 90%

Frank A. Groblewski, Jr.
Walter J. Kropp
Margaret M. Petruno
Robert M. Reynolds
Marlin B. Stetler

Designated as "Meritorious"

With General Average Between 87% and 90%

Edward N. Arshan
Edgar C. Bekes
William J. Braude
Francis J. Brocani
Eugene C. Dunham
Elmer C. Hillman
Michael Javoronok
Robert H. Lentz
Isadore Rosenthal
David M. Sherrick, Jr.

The PROCTER PRIZE, for the highest average of the class, awarded to:
MARGARET M. PETRUNO

The WILIAM B. WEBB MEMORIAL PRIZE, for the highest general average in the branches of Operative Pharmacy, Analytical Chemistry and Pharmacognosy, awarded to:

MARLIN B. STETLER

Honorable Mention to

| | |
|---|---|
| Llewellyn S. Adelman | Harold M. Gruber |
| Richard L. Boaman | Walter J. Kropp |
| Eugene C. Dunham | Margaret M. Petruno |

Robert M. Reynolds

The FRANK GIBBS RYAN PRIZE, endowed by the Class of 1884, as a memorial to their distinguished classmate, for the best average in the Chemical and Pharmaceutical Laboratory Courses, awarded to:

MARLIN B. STETLER

Honorable Mention to

| | |
|---|---|
| Eugene C. Dunham | Robert H. Lentz |
| Harold M. Gruber | Margaret M. Petruno |
| Walter J. Kropp | Robert M. Reynolds |

The MAISCH BOTANY PRIZE, offered by Sinclair S. Jacobs of the Class of 1909 to the member of the graduating class who shall have presented the best herbarium collection of plants, or the best thesis on the microscopical structure of medicinal plants, awarded to:

SAUL MALASKY

The REMINGTON MEMORIAL PRIZE, offered by the Estate of Joseph P. Remington, for the highest average in the examinations of Operative Pharmacy and Dispensing, awarded to:

MARLIN B. STETLER

Honorable Mention to

| | |
|---|---|
| Llewellyn S. Adelman | Louise A. Moffses |
| Harold M. Gruber | Robert M. Reynolds |
| Harold R. Hafer | Joseph R. Santoro |

The MAHLON N. KLINE THEORETICAL PHARMACY PRIZE, offered by the Mahlon N. Kline Estate, for the highest average in Theory and Practice of Pharmacy, awarded to:

WALTER J. KROPP

Honorable Mention to

| | |
|---|---|
| Margaret M. Petruno | Marlin B. Stetler |

The LAMBDA KAPPA SIGMA PRIZE, a Sorority Key, to the sorority member in the Ph. G. Class attaining the highest average during the Senior year, awarded to:

MARGARET M. PETRUNO

And the Sorority Key to the member making the highest average in the Senior year of the 4-year Courses, awarded to:

ELIZABETH C. ADAMS

Gold Medals awarded by the Alumni Association to the student of the Ph. G. Class and to the student of the 4-year courses who attain the highest scholastic averages, are awarded to:

Margaret M. Petruno — Saul Malasky

Window Display Prizes awarded by Sharp and Dohme:

First Prize, to

Harry A. Levenson — Claude E. Markley
Louis S. Lyon — Emanuel H. Modeck

Second Prize, to

Walter J. Kropp — Robert H. Lentz
Harry H. Levin

Third Prize, to

Cyril A. Sakalosky — David P. Secon
Arthur Scott — David M. Sherrick, Jr.

Honorable Mention to

Cecil J. P. Gray — Fred P. Ragains
Francis P. Kelly, Jr. — Robert M. Reynolds
Estelle G. Pavilonis — Michael M. Selector

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Iodine for Goiter May Produce Acne—A skin eruption resembling the acne of adolescence may follow the use of iodine for goiter prevention, it appears from a note by Dr. Karl G. Zwick of Cincinnati to Science.

This iodide acne does not occur in everyone, but does occur in persons who already have an idiosyncrasy to iodine when they start taking it as a goiter preventive, or in persons who develop sensitiveness to it.

Iodide acne seems to occur more often since the drinking water of cities is chlorinated, Dr. Zwick has observed. This is not surprising, he explains since all the halogens, the chemical group to which iodine and chlorine belong, are irritating to the glands of the skin.—*Science News.*

# MEDICAL AND PHARMACEUTICAL NOTES

FATAL POISONING WITH SODIUM NITRITE—Sodium nitrite is handled by many textile supply firms, and is distributed without poison labels to cotton mills and dye plants. We have in our laboratory stock room containers from three different manufacturing chemists bearing sodium nitrite labels, but without a poison mark of any kind.

Search of the chemical literature reveals no reported case of fatal poisoning with sodium nitrite in the United States. Two deaths in Bavaria, and four in Algeria, were attributed to sodium nitrite.

Sodium nitrite is not included in the long list of poisonous substances that the North Carolina Code specifies must be sold under poison label. Since this substance is used in large quantities in the dye rooms of many mills, we consider it wise to place on record a striking case of fatal poisoning that has occurred in North Carolina.

On October 28, 1932, we were called to investigate the death of the two-year-old son of L. D. Ray, a worker in a cotton mill in Huntersville, Mecklenburg County, N. C.

When we arrived on the scene, the child was dead. His brother directed us to the junk pile near the mill, and stated that the child picked up a small quantity of a white substance, which we saw on the junk pile, put it in his mouth, and at once ran crying toward his home, which was about 300 feet distant. Before he reached there, he fell to the ground vomiting. Members of his family hurried to him, and found him pale and weak. On picking him up his limbs hung limp, he was desperately weak, and still vomiting. He was carried directly to his home and the mill physician summoned at once. So rapid was the action of the poison that the child died before the physician arrived. His mother stated that not more than fifteen minutes had elapsed since she had picked him up.

With the aid of the physician, a portion of the stomach contents was removed. The white substance obtained from the junk pile on analysis in the laboratory proved to be sodium nitrite. Examination of the stomach contents showed that they were alkaline and contained a considerable quantitiy of sodium nitrite. The solid particles of the

stomach contents showed a distinct chocolate brown color. Stomach contents are normally acid, but the hydrolysis of a substance like sodium nitrite would cause the alkalinity. This confirms the detection of a large amount of sodium nitrite in the stomach.

To verify our opinion that sodium nitrite is a violent poison, and was the cause of this child's death, we administered 65 milligrams (1 grain) in a capsule to a cat weighing 2.6 pounds. In five minutes the cat began violent vomiting. Four minutes later it lost control of muscles, sprawled on the floor, and began screaming. The screaming slowly died down and in six minutes more, fifteen minutes after the dose was given, the cat was dead. This certainly shows the extremely poisonous nature of sodium nitrite.

Chemical literature records the two following cases of fatal nitrite poisoning:

H. Molitoris reports two cases of fatal sodium nitrite poisoning occurring within a few months in the same factory, one on October 4, 1910, and one on April 13, 1911. These were workmen in a factory where sodium nitrite was manufactured in Innsbruck, Austria.

L. Musso in 1925 reports four cases of death from sodium nitrite poisoning in a drug store in Algeria, by taking sodium nitrite from a bottle labeled "Sodium Tartrate."

The facts presented in this paper show that the use of sodium nitrite as a meat-curing agent might be attended with great danger. —*H. B. Arbuckle and O. J. Thies, Jr., Davidson College, Davidson, N. C.*

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—Ind. and Eng. Chem. N. E. July, 1933, p. 202.

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NINE KINDS OF WATER—Water is the most common, and one of the most important materials of the earth's surface. It is the prin-

cipal ingredient of our bodies and of most of our foods. Chemists find it their most useful solvent, and nature has used it most abundantly in modifying the earth we live on. What more natural than that the properties of water be used to define most of our standards, such as weight, density, viscosity and temperature? We live by water. Why not measure by it?

Until a very few years ago, no reason could be assigned for questioning the unique status of water as a material of dependable properties. Thanks to recent discoveries in science, such questioning must be done in all seriousness. In the formula of water ($H_2O$) each atom of hydrogen was found to have 1.008 units of weight and each atom of oxygen, 16.000 parts (by definition). Therefore, a molecule of water (at least in the condition of steam) should have a weight of 18.016 units. Wherever found, if sufficiently purified, water at the temperature of its greatest density was of specific gravity 1.000, froze at 0 degrees Centigrade and boiled at 100 degrees Centigrade, by definition.

Now, we know that there are two kinds of hydrogen, exactly alike in every chemical way, but the second, or newly-found "isotopic" form, is twice as heavy as the older, well-known form. Chemical compounds containing it are of course heavier by the difference in the weight of the hydrogen atoms present, so that water based on this new hydrogen should be heavier than normal. To make the matter more complex, oxygen has been found to exist as three isotopes. Ordinary oxygen is predominantly 16-unit oxygen, but contains some 17-unit and some 18-unit atoms. Water made from the heavier hydrogen and the heaviest oxygen should be materially heavier than that made from the lightest atoms. Intermediate forms of water would, in their pure form, contain in each molecule one of the heavy and one of the light isotopes of hydrogen, together with an isotope of oxygen.

Prof. G. N. Lewis, of the University of California, has very recently succeeded in concentrating the heavy form until his best sample has a specific gravity of 1.035. While this probably contains under 35 per cent. of the heaviest water, there is a great enough concentration of the new heavy water to show vividly the density difference as well as a slightly lessened refractive index. Further, the freezing and boiling points are above those of common water. The first part of the concentration of water composed of the heavier

hydrogen and oxygen atoms consists in electrolyzing large amounts of water, whereby the lighter waters are decomposed more easily than the heavier forms. While this newer water differs in all physical ways from the old, it is not to be expected that it will behave detectably different in any chemical reaction. Water is still water, but we must now specify which individual or mixture of nine possible different waters is meant when defining the basis of our standards of density, temperature, and certain other physical properties. Again science has revealed the stupendous complexity of simple things.—*Industr. Bull., A. D. Little.*

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SODIUM MORRHUATE. VARIATION IN COMMERCIAL SAMPLES. R. T. M. HAINES—An examination of five commercial samples of "sodium morrhuate 10 per cent." showed that the term is very differently interpreted, and that a standard is needed. It will be seen from the iodine values that only in sample C has an attempt been made (almost completely successful in this case) to free the drug from sodium oleate; B and D are partly purified, and A and E contain all the original oleic acid from the cod-liver oil. The determination of the iodine value of the fatty acids is important, since sodium oleate is very possibly both more toxic and less active as a sterilising agent than are the sodium salts of the more highly unsaturated fatty acids. In the subjoined table the colour values are those obtained with Lovibond's tintometer (1 cm. cell).

| Sample. | A | B | C | D | E |
|---|---|---|---|---|---|
| Appearance | Semi-solid, curdy yellow | Liquid, clear yellow | Liquid, clear orange | Liquid, turbid yellow | Gelled, turbid orange |
| Colour, yellow units | 11.8 | 18.0 | 16.0 | 9.2 | 59.6 |
| Colour, red units | 2.2 | 2.2 | 2.4 | 0.4 | 15.6 |
| Colour, general absorption | 5.4 | 0 | 0.6 | 4.8 | 13.2 |
| Total | 19.4 | 20.2 | 19.0 | 14.4 | 88.4 |
| Fatty acid content, per cent. | 9.45 | 9.03 | 9.74 | 7.0 | 8.15 |
| Iodine value, found | 178.5 | 183.9 | 241.2 | 193.5 | 169.5 |
| | Phenol per cent. | Phenol per cent. | Tricresol per cent. | Phenol per cent. | Phenol per cent. |
| Preservative in fatty acid after isolation | 3.4 | 3.5 | 2.6 | 4.9 | 3.8 |
| Iodine value, corrected | 159.3 | 164.1 | 226.5 | 165.8 | 148.0 |

—*Lancet*, 1933, 224, 748-749, through *The Analyst.*

"Spot" Tests for Some Organic Compounds—A number of macro-scale reactions of aromatic amines and aldehydes are adapted for use as "spot" tests. *Aniline* (i).—A drop of a solution of aniline salts on a filter paper moistened with saturated calcium chloride solution gives a blue-violet colour, turning red-brown, and finally disappearing. The smallest amount detectable is 1γ of aniline sulphate. If, after the blue colour has faded, the paper is held over ammonium sulphide a rose-red colour appears; 0.25γ of aniline sulphate can be detected. Benzidine, under the same conditions, gives a blue fleck; 0.02γ can be detected. Sulphanilic acid gives no colour until the paper is held over ammonium sulphide vapour, when a red coloration appears; 0.7γ can be detected. (ii) When a drop of an aniline salt solution, a drop of calcium chloride solution, and a drop of aqueous phenol are superimposed on a piece of filter paper, and the paper is held over ammonia, the edge of the drop is flecked with blue. The reaction is sensitive to 0.75γ of aniline sulphate. Sulphanilic acid gives the same reaction, benzidine does not.

*Sulphanilic Acid.*—(i) A piece of filter paper is moistened with sulphanilic acid solution, with an α-naphthylamine solution in acetic acid, and then with sodium nitrite solution. A yellow-brown red-edged fleck is formed; the test is sensitive to 0.1γ and aniline does not interfere. (ii) A drop of sulphanilic acid is treated with nitrous oxide and then with α-naphtholate solution; a red fleck is formed, sensitive to 0.02γ. Aniline gives a red-brown colour.

*Diphenylamine.*—When a drop of an alcoholic solution of diphenylamine is treated on filter paper with a dilute sulphuric acid solution of potassium dichromate, a blue fleck is formed; the test is sensitive to 0.1γ. In the presence of aniline a dark blue or green colour appears after a few minutes. Benzidine does not interfere.

*Benzidine.*—(i) An acetic acid solution of benzidine is treated on filter paper with a drop of potassium dichromate; a dark blue colour is formed, sensitive to 0.05γ. Dilute mineral acids decolorise the fleck. (ii) A drop of dilute copper sulphate solution, benzidine in acetic acid, and potassium cyanide solution, give a dark blue fleck on filter paper, sensitive to 0.1γ; aniline does not interfere. (iii) Gold chloride solution gives with benzidine on filter paper a red-brown, blue-rimmed fleck; sensitive to 0.0075γ. Other amines give similar colours.

*α-Naphthylamine.*—A drop of the hydrochloride of α-naphthylamine in solution, mixed with solution of potassium dichromate, acidified with sulphuric acid, gives a red-violet or blue fleck; sensitive to 0.3γ of α-naphthylamine hydrochloride. β-Napthylamine does not interfere.

*β-Naphthylamine.*—Filter paper strips moistened with an alcoholic solution of β-naphthylamine hydrochloride and acetic acid, and placed in furfural vapour or in an acetic acid solution of furfural, give a violet coloration, developing slowly; sensitive to 0.3γ. α-Naphthylamine does not interfere, but aniline and benzidine give a blue colour.

*Phenylhydrazine.*—A drop of a saturated solution of ammonium molybdate, followed by a drop of phenylhydrazine hydrochloride on a filter paper, and held over ammonia, gives a green-blue colour; sensitive to 0.1γ.

*Pyridine.*—A drop of a pyridine solution, followed by a drop of aniline or aniline water, and a drop of brom-cyanide (concentrated potassium cyanide solution and bromine), when placed on filter paper, give a yellow-red colour, sensitive to 0.1γ.

*Formaldehyde.*—(i) Filter paper moistened with formaldehyde solution is treated with a fragment of phenylhydrazine hydrochloride and then with a drop of sodium nitroprusside solution. On adding concentrated sodium hydroxide solution a blue evanescent colour appears. In the absence of formaldehyde the reagents give a red-yellow colour; the test is sensitive to 0.1γ. Acetaldehyde does not interfere. (ii) A drop of formaldehyde solution on filter paper (free from iron and copper) is treated with powdered phenylhydrazine hydrochloride and a drop of 5 per cent. potassium ferricyanide solution and concentrated hydrochloric acid. A red-violet fleck is formed; sensitive to 0.04γ. Acetaldehyde does not interfere. (iii) A formaldehyde solution is placed on filter paper and treated with a drop of phloroglucinol solution, and then with dilute sodium hydroxide solution. A red-brown fleck is formed; sensitive to 0.03γ.

*Acetaldehyde.*—When a drop of acetaldehyde solution, piperidine, and sodium nitroprusside solution are placed on filter paper, a rim of blue is formed, changing to red with alkali; sensitive to 0.4γ. Formaldehyde does not interfere. Acetone gives a light red colour.

*Furfural.*—When treated with a solution of aniline in 80 per cent. acetic acid (1:1) a blue colour is formed; sensitive to 0.05γ. The reactions with benzidine and α-naphthylamine are not so sensitive.

*Vanillin.*—A drop of alcoholic vanillin solution, when treated with a drop of phloroglucinol in concentrated hydrochloric acid, gives an orange fleck, turning red; sensitive to 1γ.—I. M. Korenman, *J. Chem. Ind.* (Russ.), 1931, 8, 508-510; *Mikrochem.*, 1932, 11, 473-475, through the *Analyst.*

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Chemical-Pharmaceutical Industry Well Developed in Russia—One of the few branches of the chemical industry that has actually exceeded the requirements of the five-year plan is that dealing with pharmaceuticals. This is shown in the following table in price levels of 1926-27:

| | *Planned Production Million Rubles* | *Actual Production Million Rubles* |
|---|---|---|
| 1928 | 44.1 | 27 |
| 1929 | 48.0 | 42 |
| 1930 | 50.0 | 48 |
| 1931 | 66.4 | 57 |
| 1932 | 60.0 | 110 |

Besides the production of pharmaceuticals, this industry also undertook the manufacture of certain purely chemical preparations. Through the scientific institute devoted to the drug industry, the production of acetylsalicylic acid has been improved, and the manufacture of pyramidone has become feasible. Progress has also been made during the past few years in the manufacture of silver, mercury, bromo-, iodo-, bismuth, and arsenic preparations, of alkaloids, guaiacol, and salicyl derivatives, benzoic and lactic acids, and hexamethylene tetramine.

As early as 1929-30, alkaloids were produced in the following amounts per annum: cocaine, 1.22 tons; pantopan, 0.24 ton; morphine hydrochloride, 0.63 ton; codeine, 2.88 tons; ethylmorphine hydrochloride, 0.44 ton; and diacetylmorphine, 0.12 ton. In 1932, the production of iodine and bromine was 80 and 200 tons, respectively.

Attempted cultivation of cinchona species was undertaken in 1931, in the Northern Caucasus. In Leningrad a plant for producing camphor, with an annual capacity of 400 tons per annum, has been erected.

Ever since 1882 Russia has extracted santonin from wormseed, large amounts of which are found in the wide steppes of Turkistan and furnish the raw material for a factory in Tschimkent. In 1930, the export of santonin reached 9.4 tons, but in 1931 shrank to 3.6 tons.—News Edition, *Jour. Ind. & Eng. Chem.*, June, 1933, p. 195.

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Summary of Changes in the Proposed New Food and Drugs Act—Drugs considered dangerous to health are deemed adulterated.

Secretary of Agriculture may prescribe methods of testing U. S. P. or N. F. products when such tests are not given, or may add to tests when he so desires.

Cosmetics are included in the act and may be deemed adulterated if considered dangerous to health, or if they contain poisonous or deleterious substances.

Drugs and cosmetics must bear content statement on label.

Labels of drugs may bear names of diseases for which products are not specifics, but are merely palliatives, if a statement that the drug is not a cure is made.

Drug is misbranded if the label contains statement contrary to general medical opinion.

Drug is misbranded if not packaged or labeled in form and manner prescribed by Secretary of Agriculture for the prevention of deterioration of those drugs subject to deterioration.

Drug is misbranded if the container is made, formed or filled to mislead purchasers; if it is an imitation of another drug; if it is offered for sale under the name of another drug.

Antiseptics and germicides must give on labels for each use the method and duration of application necessary to kill all micro-organisms in the vegetive or other active form with which it comes in contact when so used; or there must be given on label the specific micro-organisms which the product affects together with the conditions, duration of application under which the product kills all such micro-organisms.

Drug and cosmetic advertising is regulated so that statements must conform to facts as in the case of label statements.

Drug advertising is further regulated so that no advertising to other than the medical and pharmacological professions is allowed for products claimed to have any effect upon any of a long list of diseases written in the bill; and further empowering the Secretary of Agriculture, as he sees fit, to add to the list of diseases in which self-medication is dangerous, and prohibiting consumer advertising of products claimed to affect such diseases.

Permits are required for factories producing those classes of drugs and cosmetics which Secretary of Agriculture deems may be injurious to health, when the Secretary feels that such danger cannot be ascertained after such articles have entered interstate commerce.

Inspectors of the department are to inspect drug and cosmetic factories with the permission of the owners. District courts are granted power of injunction against shipment of goods from those factories which do not permit inspection.

Manufacturers may request inspection of their plants at cost, and then use on labels fact that they have been inspected by Government and found to be in conformity with law.

Secretary of Agriculture will draw up entire regulations for enforcement of the act with the exception of that relating to imports in which the Secretary of Treasury shall concur. Regulations for the present act are drawn up by the three Secretaries of Agriculture, Commerce and Treasury.—*The Drug & Cosmetic Industry,* June, 1933.

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THE CAMPHOR OF COMMERCE—There are two chief sources of the commercial supply of camphor—Japan and Germany—but synthetic camphor is now being made in America by the du Pont Company. The water-white liquid is ordinarily prepared from what is commonly called "camphor gum," which is not a gum but a crystalline substance. Pharmacists use it; curators know its value; housewives find it a household necessity; but the greatest amount of camphor finds its way into the manufacture of industrial products. Camphor is an indispensable raw material in the pyroxylin plastic industry. As a plasticizing agent in transforming cellulose into "pyralin" and

photographic film, nothing better has been found so far. For centuries practically all the natural camphor used in the United States was imported from China, Japan, the East Indies, Formosa, and other eastern lands where the camphor forests are abundant; but since 1899 practically all the world's supply of natural camphor has been controlled by the Japanese government. For years American manufacturers had to battle a Japanese monopoly. In 1880 the Department of Agriculture imported camphor berries and young trees from Japan and planted them in southern and southwestern states. These attempts had to be abandoned because of the World War. Controlled prices after the war brought the question of synthetic camphor sharply into focus. In 1803 an apothecary by the name of Kindt introduced HCl into oil of turpentine and obtained a crystalline product resembling camphor, but in reality it was boronyl chloride. Bertholet, a French chemist, is said to have been the first to produce a chemically made camphor. This was in 1858. Others made contributions; but the synthetic product caused little uneasiness in Japan until late in the first decade of this century when European competition threatened Oriental monopoly. In 1923, there were imported 3,240,322 pounds of refined camphor at a value of $0.735 per pound as against 488,684 pounds of synthetic valued at $0.619 per pound. In 1932, there were imported 941,459 pounds at $0.353 per pound as against 1,416,331 pounds synthetic camphor valued at $0.278 per pound. Camphor gathering has been and still is in some regions a risky business. The savages in the hinterland of Formosa, where the trees grow, are head hunters. Today trained operators get everything out of the wood that is valuable, and in Japan a reforestation program insures a future supply of trees. While Germany was busy breaking down the Japanese monopoly, American chemical concerns were inactive; but as early as 1900 one American concern started production at Niagara Falls. Others followed, only to drop by the wayside. Today, however, synthetic camphor is being manufactured by a new du Pont process from southern turpentine. Apparently this is the only attempt in America to manufacture "synthetic" camphor of high quality in quantity to supply our domestic needs. "Synthetic" is really a misnomer for the product is not built up from simple elements but starts with a complex organic substance. It is a strange coincidence that the basic material for this product also comes from a tree—the southern pine.—*Anon. Du Pont Mag.*, 27, 1-3, 15-16 (Apr., 1933) through *Jour. Chem. Educ.*

SODIUM AMYTAL IN STRYCHNINE POISONING—The modern treatment of strychnine poisoning consists chiefly and pre-eminently in the intravenous administration of sodium amytal, either during the premonitory stage or when the convulsion has begun. The dose is 7½ grains (0.5 gm.). Smaller or larger doses to be used as required and repeated with each convulsion. In severe cases, when repeated injections of the barbiturates are required, they may be supplemented with tribrom-ethanol anesthesia. Giving a chemical antidote, such as tannic acid, and lavage of the stomach are also important. Chloral and bromides may also be given.

To date, eleven cases have been reported of human strychnine poisoning treated successfully with sodium amytal.—*Stalberg* and *Davidson, Jour. A. M. A.*, July 8, 1933, p. 104.

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NON-SULFIDE DEPILATORIES—Alkali stannites are used as active ingredients in preparing depilatories. Many objectionable features of sulfides in depilatories are overcome. New preparations are non-toxic, non-irritating, effective, rapid in action, stable in air, light in color (even pure white) and odorless or easily perfumed. Sodium stannite is highly effective and is used with suitable wetting agents to aid in penetration of active principle. Pure soap, preferably sodium oleate, is preferred. Inert fillers, such as natural white clays, white diatomaceous earth, alkali earth silicates, for example magnesium silicate, are also used. Fillers act as buffers and reduce any caustic action of depilatory on skin.—*Drug & Cosmetic Industry*, June, 1933.

# BOOK REVIEW

URINE AND URINALYSIS. By Louis Gershenfeld, Ph. M., B. Sc., P. D. Professor of Bacteriology and Hygiene and Director of the Bacteriological and Clinical Chemistry Laboratories at the Philadelphia College of Pharmacy and Science. 12mo, 272 pages, illustrated with 36 engravings. Published, 1933. Limp binding, $2.75 net, Lea & Febiger, Philadelphia, Pa.

Written by one who has had a large experience in teaching as well as in performing the work described in the book, this handy volume should be eminently practical and dependable. Generally speaking the laboratory manuals on urinalysis have been altogether too terse and brief—except in those few cases where they err in the direction of toomuchness.

This work affords the happy medium—compact, complete and certainly up-to-date. And furthermore it is specific to its subject.

It has been specially written for graduates in pharmacy, chemistry, bacteriology and the allied professions; for nurses and technicians and for those general practitioners in medicine whose interest in this subject centers about the performance of urinalyses.

The author writes from a long experience which has included the personal performance of over 25,000 urinalyses, and the supervision of many times that number. He presents the subject in all its aspects, including the laboratory methods of examination, the nature of cases in which abnormal findings prevail, and the interpretations of the examinations suggested. The work is conveniently organized and an orderly arrangement of the material is maintained throughout.

The up-to-dateness of the work is particularly evident—as, for instance, in the chapter on nitrogen retention and kidney function tests.

A number of brand new and original illustrations relieve this book of the criticism so often made that authors of such books are too wont to use time-honored and trite cuts borrowed from other sources, in order to minimize illustration costs.

The printing and binding are well done—and the work is singularly free from typographical and other errors.

Altogether one feels that this is a helpful book, sensibly and accurately written, not compiled just to please a whim, but rather to fill a real need. In its particular field there is no book quite its equal.

IVOR GRIFFITH.